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REMARKS/ARGUMENTS

Each of the matters in the Office Action will be responded to below.

a. Response to Objection to Claim 3 under 37 CFR 1.75(c)

Claim 3 was objected to under 37 CFR 1.175(c), as being of improper dependent form for failing to further limit the subject matter of Claim 1.

In response to the objection, Applicant has amended Claim 3 to recite "applying said treatment composition by hypodermic injection". The amended language further limits Claim 1 (from which Claim 3 depends) by limiting the manner in which the treatment composition is introduced to the body, i.e., it is introduced beneath the skin of the patient (see Attachment 1, definition from *The Shorter Oxford English Dictionary*). By comparison, Claim 2 limits the method to introduction by topical application of the treatment composition.

Descriptive support for the new claim language is found at page 4, lines 21-22 and page 6, lines 10-12 of the Application as originally filed, wherein it is described that the treatment composition may be introduced directly into the sub-dermal tissues.

Accordingly, it is respectfully submitted that the objection to Claim 3 under 37 CFR 1.75(c) has been overcome by the present amendment.

b. Response to Rejection of Claim 42 Under 35 USC §112

Claim 42 was rejected under 35 USC § 112, second paragraph, as being indefinite, on grounds of lacking antecedent basis for "said organogel compound."

By the present amendment, Applicant has amended Claim 42 to depend from Claim 41, which contains antecedent basis for the term "organogel compound."

Accordingly, it is respectfully submitted that the rejection of Claim 42 under 35 USC §112 has been overcome by the present amendment.

c. Response to Rejection of Method Claims Under 35 USC §102

The method claims presently in the Application are Claims 1-3, 8-9, and 23-32. Claims 23-32 are allowed. The remaining method claims were rejected under 35 USC § 102(b) as follows:

Claims 1, 2 and 8 were rejected as being anticipated by Chemical Abstracts 132:69251.

Claims 1, 2 and 8 were rejected as being anticipated by Chemical Abstracts 100:73895.

Claims 1 and 3 were rejected as being anticipated by Chemical Abstracts 85:87225.

By the present amendment, Applicant has amended the rejected method claims to distinguish over the cited references. Specifically, independent Claim 1, from which the other rejected method claims depend, has been amended to recite that the method is limited to the treatment of musculoskeletal soft tissue. The term "sub-dermal" has therefore been deleted and replaced with "musculoskeletal" throughout Claim 1 and also in Claims 2-3. Furthermore, Claim 1 has been amended to expressly recite that the claimed method includes the step of "determining a localized area of a patient's body in which affected musculoskeletal soft tissue is located", and "applying said treatment composition to said localized area of said patient's body so that said macrolide antibiotic penetrates said affected musculoskeletal soft tissue". Support for the added limitations is provided at page 5, lines 8-12 of the Application as originally filed.

None of the references teaches a method for alleviating a disease state resulting from a microbial infection affecting musculoskeletal soft tissue, as is required by amended Claim 1. Chemical Abstracts 132:69251 and Chemical Abstracts 100:73895 are both directed to acne, while Chemical Abstracts 85:87225 is directed to skin syphilomas, all of which are conditions involving the skin as distinct from the musculoskeletal system. With regard to Chemical Abstracts 132:69251, the Examiner noted the statement therein that "infiltration of the antibiotics into the affected s.c. [subcutaneous] layers is highly desirable"; since acne is a condition of the skin, it is clear that the statement made in Chemical Abstracts 132:69251 with regard to

infiltration of "s.c. layers" refers to the subcutaneous layers of the skin (see Attachment 2, excerpt from AMA *Atlas of the Body*), not to the tissues of the musculoskeletal system.

Moreover, none of the references show the steps of (a) determining a localized area of the body in which affected muscular soft tissue is located, and (b) applying the treatment composition to the localized area so that the macrolide antibiotic penetrates the affected musculoskeletal soft tissue, as are also expressly required by amended Claim 1 and its dependents.

The Examiner noted that Chemical Abstracts 132:69251 states that erythromycin was detected in the underlying muscles. However, there is no correlation between the acne (to which the composition of Chemical Abstract 132:69251 is applied) and the area or areas of the body in which musculoskeletal tissue affected by chlamydia, microplasma and/or other microorganisms (as described in Applicant's specification) is located. Chemical Abstracts 132:69251 consequently does not teach applying the treatment composition to a localized area of the body in which the affected musculoskeletal tissue is located, as is expressly required by Applicant's claims.

Similarly, there is no correlation between the areas of the skin syphilomas of Chemical Abstracts 85:87225 and the location of affected musculoskeletal tissue to which the treatment of the invention is directed. The Examiner noted that tertiary syphilis, with which skin syphilomas are associated, involves other parts of the body (organs, central nervous system, bones) besides the skin; Chemical Abstracts 85:87225 contains no suggestion that its purpose is to treat areas of the body other than the skin, however, it is clear that the treatment is applied on a systemic basis, not to a localized area of the body as required by Applicant's claims. Moreover, the reference does not show a treatment composition that includes a mobilizing agent that enables the macrolide antibiotic to penetrate into the musculoskeletal soft tissue, as is also required by Applicant's claim 1. In the Office Action, the Examiner asserted that in Chemical Abstracts 85:87255 a "pharmaceutical carrier is necessarily present in an intramuscular injection, and such carrier meets the mobilizing agent claim feature." Applicant respectfully disagrees: In order for the erythromycin to have reached the skin syphilomas it must have been withdrawn from the site of the intramuscular injection and into the bloodstream; it does not follow from this that the carrier is a mobilizing agent that enables the macrolide antibiotic to penetrate into the musculoskeletal tissue. In short, the purpose of the intramuscular injection in Chemical

Abstracts 85:87225 is simply to introduce the erythromycin in a manner such that it will be carried by the bloodstream to the skin syphilomas, and has nothing to do with penetrating into and treating the soft tissue proximate the injection site itself.

In order to anticipate a claim, the reference must show each and every element that is contained in the claim (MPEP 2131). For the reasons explained above, none of the cited references--Chemical Abstracts 132:69251, Chemical Abstracts 100:73895, Chemical Abstracts 85:87225--show a method for alleviating a disease state resulting from a microbial infection affecting musculoskeletal soft tissue, that includes the steps of (a) determining a localized area of the patient's body in which affected musculoskeletal soft tissue is located and (b) applying to the localized area of the body a treatment composition that includes a macrolide antibiotic and a mobilizing agent so that the antibiotic penetrates into the affected musculoskeletal tissue, as is expressly required by claim 1 and its dependents. Accordingly, Applicant respectfully submits that the references fail to anticipate amended Claim 1 and its dependent Claims 2-3 and 8-9, and that the rejections of the method claims under 35 USC §102 have therefore overcome by the present amendment.

d. Response to Rejection of Composition Claims under 35 USC §102

The composition claims presently in the Application are Claims 10, 12-23 and 33-42. Claims 18-26 and 38-41 are allowed. Claim 42 was rejected under 35 USC §112, but has been corrected as noted above. Claims 9, 15,17, 35 and 37 were objected to as being dependent on a rejected base claim. The other method claims were rejected under 35 USC §102(b) as follows:

Claims 10, 12, and 16 were rejected as being anticipated by Chemical Abstracts 132:629251.

Claims 10, 13, 16, 33, and 36 were rejected as being anticipated by Oh et al.

Claims 10, 12, and 14 were rejected as being anticipated by Chemical Abstracts 100:73895.

Claims 10, 12-14 and 33-34 were rejected as being anticipated by Kornman (WO 95/09601).

By the present Amendment, Applicant has amended the rejected composition claims to distinguish over the cited references. Specifically, independent composition claims 10 and 33

have been amended to expressly recite that the composition comprises "a selected organic gel compound in an amount sufficient to enable said macrolide antibiotic to penetrate into said musculoskeletal soft tissue". Claims 14 and 34 have been amended to correspond to the revised language of the independent claims (in addition, Claim 15 has been amended to correct an error in dependency).

Of the cited references, Chemical Abstracts 132:69251 and Oh et al. do not show any compositions that comprise an organic gel. With regard to the remaining two references, Chemical Abstracts 100:73895 shows a composition that includes a hydrogel of methylcelulose and Kornman shows a gel containing hydroxypropylmethylcelulose, however, neither reference shows use of an organic gel "in an amount sufficient to enable a macrolide antibiotic to penetrate into musculoskeletal soft tissue" as required by Claims 10 and 33: As has been discussed above, Chemical Abstracts 100:73895 is directed to treatment of acne, which is limited to the skin. Kornman, in turn, discloses a composition for treating periodontitis resulting from dental plaque and calculus, which involve deposits and bacterial activity along the surfaces of the teeth above and below the gumline (see Attachment 3, excerpt from US Navy training manual, *Dental Technician, Vol. 2*). Consequently, neither shows the use of a mobility agent to penetrate into muscles and other musculoskeletal soft tissue.

Furthermore, none of the references shows a treatment composition comprising a penetration enhancing adjuvant in combination with an organic gel mobilizing agent, as is required by dependent composition Claims 16-17 and 36-37. In the Office Action, the Examiner asserted that in Oh et al. the "Triton X-100 meets the claimed "penetration enhanding adjuvant feature". Applicant respectfully disagrees: in Oh et al., the Triton X-100 is not a part of the composition, and is instead used to dissolve samples of the product for assay to determine azithromycin concentrations (page 2105, bottom of left-hand column). With regard to Chemical Abstracts 100:73895, it was asserted that "the Examiner has sufficient basis for determining the solvent in surface-active functioning substances such as Tween 80, cetylstearyl alcohol and triethanolamine as meeting the claimed feature of penetrating enhancing adjuvant." Applicant respectfully traverses this assertion as well: The Tween 80, cetasteryl alcohol and triethlymine of Chemical Abstracts 100:73895 are all well known emulsifiers and thickeners, used especially in the cosmetics industry (Attachment 4 and 5, exerpts from *Merck Index* and *Dorland's Medical Dictionary*), which chararacteristics would appear consistent with aiding penetration of

musculoskeletal soft tissue; in these and other characteristics the compounds, are distinctly different from the d-limonine, terpenes, DMSO and other penetration enhancing adjuvants listed in the present application (Attachment 6, excerpts from *Merck Index*). Consequently, Applicant respectfully submits that sufficient basis does not exist to conclude that the Tween 80, cetasterol alcohol and triethylmine of Chemical Abstracts 100:73895 meet the claimed feature of a penetration enhancing adjuvant.

Accordingly, for the reasons explained above, none of the cited references discloses a treatment composition which comprises a "mobilizing agent comprising a selected organic gel compound in an amount sufficient to enable said macrolide antibiotic to penetrate into said musculoskeletal soft tissue", as is expressly required by amended independent Claims 10 and 33. Applicant therefore respectfully submits that the references do not anticipate Claims 10 and 33 and their dependent claims 12-17 and 34-37, and that the rejections of the composition claims under 35 USC §102 have consequently been overcome by the present Amendment.

e. Other Amendments

The term "compound" in Claim 40 has been amended to read "composition", thus correcting a typographical error.

f. Conclusion

Applicant respectfully requests reconsideration of the present Application in view of the amendments and remarks set forth herein. It is believed that the above-referenced claims are now in condition for allowance. If there is any matter that can be expedited by consultation with Applicant's attorney, such would be welcome. Applicant's attorney can normally be reached at the telephone number given below.

Signed at Bellingham, County of Whatcom, State of Washington this 27th day of August 2004.

Respectfully submitted,

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By _____

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below', f. ὑπό HYPO- 1 + καυ-, καίειν to burn.] *Rom. Antiq.* A hollow space extending under the floor of the *caldarium*, in which the heat from the furnace (*hypocausis*) was accumulated for the heating of the house or of a bath. **b.** *transf.* A stove. SCOTT.

Hypochlorite (həipoklō·rəit). 1835. [HYPO- 5.] *Chem.* A salt of hypochlorous acid.

Hypochlorous (həipo-, hipoklō·rəs), *a.* 1841. [HYPO- 5.] *Chem.* *H. acid*, an oxy-acid of chlorine (HClO), which possesses strong oxidizing and bleaching qualities.

Hypochonder, -chondre (hipokǫ·ndəɹ). ? *Obs.* 1547. [a. F. *hypocondre*; see next.] = HYPOCHONDRIUM. Also *pl.* = HYPOCHONDRIA 1.

Hypochondria (həipokǫ·ndriă, hipo-). 1563. [ad. late L. *hypochondria* pl., a. Gr. τὰ ὑποχόνδρια, neut. pl. of ὑποχόνδριος, f. ὑπό HYPO- 1 + χόνδρος cartilage, esp. that of the breast-bone.] ‖ 1. as pl. of HYPOCHONDRIUM. Those parts of the human abdomen which lie immediately under the ribs and on each side of the epigastric region. †**b.** The viscera situated in the hypochondria; the liver, gall-bladder, spleen, etc., formerly supposed to be the seat of melancholy and 'vapours' -1652. †**c.** Erron. as *sing.* -1727. **2.** as *sing.* General depression, melancholy, or low spirits, for which there is no real cause 1668.

2. Will Hazard was cured of his h. by three glasses 1710. Hence **Hypocho·ndrial** *a.*

Hypochondriac (həipokǫ·ndriæk, hipo-). 1615. [a. F. *hypocondriaque*, ad. med.L. *hypochondriacus*; see prec.]

A. *adj.* **1.** Of states: Proceeding from the hypochondria, regarded as the seat of melancholy; hence, consisting in a settled depression of spirits. ? *Obs.* **b.** Of persons, their dispositions, etc.: Affected by hypochondria 1641. **2.** *Anat.* Situated in the hypochondria 1727. *H. region*, the part of the abdomen occupied by the hypochondria. 1727.

1. b. Complaints founded only in an h. imagination 1782.

B. *sb.* **1.** A person affected with or subject to hypochondria 1639. †**2.** = HYPOCHONDRIA 2. -1796.

2. Abbreviations exquisitely refined: as..Hypps, or Hippo, for Hypochondriacks SWIFT.

So **Hypochondri·acal** *a.* = prec. A. **Hypochondri·acally**, *adv.* **Hypochondri·acism** = HYPOCHONDRIA 2.

Hypochondriasis (həi:po,kǫndrəi·ăsis, hi:po-). 1766. [f. HYPOCHONDRIA + -ASIS. But the suffix *-asis* is almost entirely limited to names of cutaneous diseases.] *Path.* A disorder of the nervous system, generally accompanied by indigestion, but chiefly characterized by the patient's unfounded belief that he is suffering from some serious bodily disease. So **Hypocho·ndriasm** (in same sense). **Hypocho·ndriast** = HYPOCHONDRIAC *sb.* 1.

Hypocho·ndric, *a. rare.* 1681. [f. as prec. + -IC.] = HYPOCHONDRIAC *a.*

‖**Hypochondrium** (həipokǫ·ndriǒm, hi·po-). 1696. [mod.L., ad. Gr. ὑποχόνδριον; see HYPOCHONDRIA.] Each of the two hypochondriac regions which are distinguished as 'right' and 'left'.

†**Hypocho·ndry.** 1621. [ad. L. *hypochondrium, -ia.*] **1.** = HYPOCHONDRIUM. Chiefly *pl.* -1685. **2.** = HYPOCHONDRIA 2. -1874.

†**Hy·pocist.** 1751. [Cf. F. *hypociste.*] = next.

†**Hypocistis.** 1425. [a. L., a. Gr. ὑποκιστίς, f. ὑπό + κίστος the plant Cistus. (The early forms *h)ypoquistid(os* represented the Gr. genitive.)] *Med.* The solidified juice of *Cytinus hypocistis*, a parasitic plant of the South of Europe, growing on the roots of Cistus; it contains gallic acid, and was formerly used as a tonic and astringent -1751.

Hypocorism (həip-, hipǫ·kŏriz'm). *rare.* 1850. [ad. Gr. ὑποκόρισμα, -κορισμός, f. ὑποκορίζεσθαι to play the child, f. ὑπό + κόρη.] A pet-name.

Hypocoristic (həi:po-, hi:pokŏri·stik), *a.* 1796. [ad. Gr. ὑποκοριστικός; see prec.] Of the nature of a pet-name; pertaining to the habit of using endearing or euphemistic terms.

Harry..is the free or h. name for Henry PEGGE. So †**Hypocori·stical** *a.* 1609, -ly *adv.* 1652.

Hypocotyl (həipo-, hipo,kǫ·til). 1880. *Bot.* Name for the hypocotyledonous stem. Hence **Hypoco·tylous** *a.*

Hypocotyledonary (həi:po-, hi:po,kǫtilī·dŏnări), *a.* 1875. [HYPO- 2.] Placed under, or supporting, the cotyledons. So **Hypocotyle·donous** *a.*

Hypocrateriform (həi:po-, hi:po,krătī·rifǭɹm), *a.* 1760. [f. Gr. ὑποκρατήριον (f. ὑπό HYPO- 1 + κρατήρ CRATER 1) + -FORM.] *Bot.* Having the form of a salver raised on a support: said of a corolla in which the tube is long and cylindrical, with a flat spreading limb at right angles to it, as the periwinkle and phlox. So **Hypocrate·rimorphous** *a.*

‖**Hypo·crisis.** ME. [L.; see next.] Hypocrisy.

Hypocrisy (hipǫ·krĭsi). ME. [a. OF. *ypocrisie* (mod. *hypocrisie*), f. eccl. L. *hypocrisis*, a. Gr. ὑπόκρισις, f. ὑποκρίνεσθαι to answer, play a part, pretend, f. ὑπό HYPO- + κρίνειν to decide, judge.] The assuming of a false appearance of virtue or goodness, with dissimulation of real character or inclinations, esp. in respect of religious life or belief; hence, dissimulation, pretence, sham. Also, an instance of this.

It is the law of goodness to produce h. MOZLEY.

Hypocrite (hi·pŏkrit). ME. [a. OF. *ypo-*, *ipocrite* (mod. *hypocrite*), ad. eccl. L. *hypocrita*, ad. Gr. ὑποκριτής an actor, pretender, f. ὑποκρίνεσθαι; see prec.] One who falsely professes to be virtuously or religiously inclined; one who pretends to be other and better than he is; hence, a dissembler, pretender. Also *attrib.* or *adj.*

Woe vnto you, Scribes and Pharisees, hypocrites *Matt.* xxiii. 13. Her cousins, seeing her with red eyes, set her down as a h. JANE AUSTEN. *attrib.* H. fanatics SWIFT. Hence **Hypo·crital** *a.* (now *rare*), hypocritical. †**Hy·pocritely** *a.* and *adv.*

Hypocritic (hipŏkri·tik). 1540. [ad. Gr. ὑποκριτικός; see HYPOCRISY.]

A. *adj.* = HYPOCRITICAL.

His silken smiles, his h. air CHURCHILL.

B. *sb. rare.* **1.** = HYPOCRITE 1818. †**2.** The art of declamation with appropriate gesture. BURNEY.

Hypocritical (hipŏkri·tikăl), *a.* 1538. [f. as prec. + -AL.] Of the nature of, characterized by, hypocrisy; (of persons) addicted to hypocrisy.

They are exceedingly subtill, hypocriticall and double-dealing PURCHAS. Formal or h. professions FREEMAN. Hence **Hypocri·tically** *adv.* 1548.

Hypocycloid (həipo-, hiposəi·kloid). 1843. [HYPO- 2.] *Geom.* A curve traced by a point in the circumference of a circle which rolls round the interior circumference of another circle (cf. EPICYCLOID). Hence **Hypocycloi·dal** *a.*

Hypoderm (həi·po-, hi·podə̄ɹm). 1855. [ad. next.] = HYPODERMA 1.

‖**Hypoderma** (həipo-, hipodə̄·ɹmă). *Pl.* -**dermata.** 1826. [mod.L., f. Gr. ὑπό + δέρμα skin; cf. HYPODERMIS.] **1.** *Zool.* A tissue or layer lying beneath the skin or outer integument in Arthropoda and other invertebrates; 'the subcutaneous areolar tissue of the skin of mammals' (*Syd. Soc. Lex.*). **2.** *Bot.* A layer of cells lying immediately under the epidermis of a leaf or stem 1877. Hence **Hypode·rmal** *a.*

Hypodermatic (həi:po-, hi:po,dəɹmæ·tik), *a.* 1855. [HYPO- 2.] = HYPODERMIC. Also as *sb.* = hypodermic injection. Hence **Hypoderma·tically** *adv.*

Hypodermic (həipo-, hipodə̄·ɹmik), *a.* 1865. [f. HYPODERMA + -IC.] **1.** *Med.* Pertaining to the use of medical remedies introduced beneath the skin of the patient; esp. in *h. injection*, the introduction of drugs into the system in this manner. **b.** as *sb.*: A hypodermic remedy 1875. **2.** *Anat.* Lying under the skin; pertaining to the hypoderm 1877. Hence **Hypode·rmically** *adv.* subcutaneously.

‖**Hypodermis** (həipo-, hipodə̄·ɹmis). 1866. f. HYPO- 2 + Gr. -δερμις, *-dermis* as in EPIDERMIS.] **1.** *Bot.* The inner layer of the spore-case of an urn-moss. **2.** *Zool.* = HYPODERMA 1. 1874.

Hypogæic, etc.: see HYPO-.

Hypogastric (həipo-, hipogæ·strik). 1656. [ad. F. *hypogastrique*, f. *hypogastre*; see next.] **A.** *adj.* Pertaining to, or situated in, the hypogastrium. *H. region* = HYPOGASTRIUM. So †**Hypoga·strical** *a.* 1615. †**B.** *sb. pl.* The hypogastric arteries (*rare*) 1722-1797.

‖**Hypogastrium** (həipo-, hipogæ·striǒm). 1681. [mod.L., ad. Gr. ὑπογάστριον, f. ὑπό + γαστήρ, γαστρ- belly.] The lowest region of the abdomen; *spec.* the central part of this, lying between the iliac regions. So **Hypoga·strocele** (*Path.*), a hernia in the hypogastric region.

Hypoge·al, *a.* 1686. [f. as next + -AL.] = next.

Hypogean (həipo-, hipodʒī·ăn), *a.* 1852. [f. L. *hypogeus*, ad. Gr. ὑπόγειος (f. γῆ earth) + -AN.] Existing or growing underground; subterranean.

Hypogene (həi·po-, hi·podʒīn), *a.* 1833. [f. HYPO- 2 + Gr. γεν-, γίγνεσθαι. Cf. F. *hypogène.*] *Geol.* Formed under the surface; applied to rocks otherwise called primary and metamorphic; also, subterranean, hypogean. Hence **Hypoge·nic** *a.*

Hypogeous (həipo-, hipodʒī·əs), *a.* Also -**gæous.** 1847. [f. as HYPOGEAN + -OUS.] = HYPOGEAN.

‖**Hypogeum** (həipodʒī·ǒm, hipo-). Also -**gæum.** *Pl.* -**gea** (-ʒī·ă). 1706. [L. *hypogeum*, *hypogæum*, ad. Gr. ὑπόγειον, ὑπόγαιον adj. neut. sing. used subst.; see HYPOGEAN.] An underground chamber or vault. var. **Hy·pogee** (*rare*) 1656.

Hypoglossal (həipo-, hipoglǫ·săl), *a.* 1831. [f. mod.L. HYPOGLOSSUS + -AL.] *H. nerve*, the motor nerve of the tongue proceeding from the medulla oblongata and forming the twelfth or last pair of cranial nerves. Also *absol.* = HYPOGLOSSUS.

‖**Hypoglossus** (həi·po-, hipoglǫ·sǒs). 1811. [mod.L., f. Gr. ὑπό + γλῶσσα tongue.] *Anat.* The hypoglossal nerve.

Hypogyn (həi·po-, hi·podʒin). 1847. [ad. F. *hypogyne.*] *Bot.* A hypogynous plant. So **Hypogy·nic** *a.* = next.

Hypogynous (həip-, hipǫ·dʒinəs), *a.* 1821. [f. mod.L. *hypogynus* (1789), f. Gr. ὑπό + γυνή taken as = 'pistil' + -OUS.] *Bot.* Situated below the pistils or ovary; said of stamens when these grow on the receptacle and are not united to any other organ; also of plants having the stamens so placed. So **Hypo·gyny**, h. state.

Hyponasty (həi·po-, hi·pŏnæsti). 1875. [f. HYPO- 2 + Gr. ναστός pressed + -Y. Cf. EPINASTY.] *Bot.* A tendency in plant-organs to grow more rapidly on the under or dorsal side than on the upper or ventral. Hence **Hypona·stic** *a.* pertaining to or characterized by h.

†**Hyponitric** (həipo-, hiponəi·trik), *a.* 1854. [HYPO- 5.] *Chem.* In *h. acid*, an old name for tetroxide (or peroxide) of nitrogen, pernitric acid, NO_2 or N_2O_4 -1876.

Hyponitrite (həipo-, hiponəi·trəit). 1836. [HYPO- 5.] *Chem.* A salt of hyponitrous acid.

Hyponitrous (həipo-, hiponəi·trəs), *a.* 1826. [HYPO- 5.] *Chem.* In *h. acid*, an unstable acid $(HNO)_2$, obtained in combination as a potassium salt.

Hypopharynx (həipo-, hipofæ·riŋks). 1826. [a. F., f. HYPO- 2 + PHARYNX.] *Entom.* A median projection from the internal surface of the lower lip in insects. Hence **Hy·pophary·ngeal** *a.* situated beneath, or in the lower part of, the pharynx; belonging to the h.

Hypophosphate (həipo-, hipofǫ·sfĕt). 1864. [HYPO- 5.] *Chem.* A salt of hypophosphoric acid.

Hypophosphite (həipo-, hipofǫ·sfəit). 1818. [HYPO- 5.] *Chem.* A salt of hypophosphorous acid.

THE
SHORTER OXFORD
ENGLISH DICTIONARY

ATTACHMENT 2

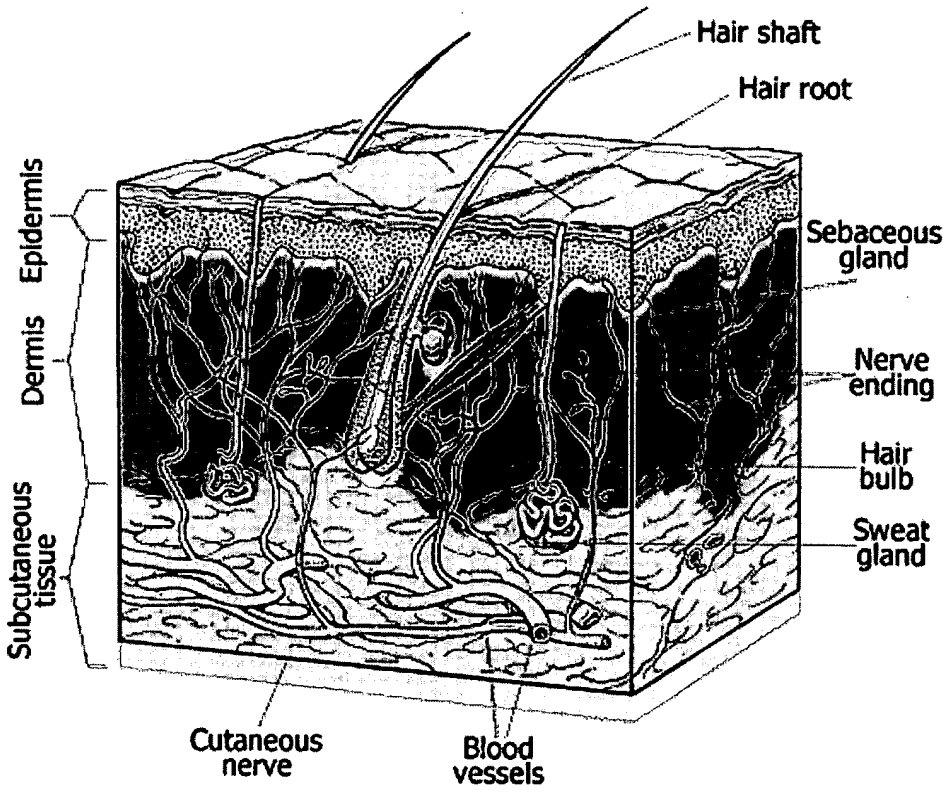
Medical Library

Printer-friendly format

American Medical Association

Atlas of the Body: The Skin

The skin — the largest organ of the body — is made up of a thin outer layer (called the epidermis) and a thicker outer layer (called the dermis). Below the dermis is the subcutaneous tissue, which contains fat. Buried in the skin are nerves that sense cold, heat, pain, pressure, and touch. Sebaceous glands secrete a lubricating substance called sebum. Deep within the skin are your sweat glands, which produce perspiration when you are too hot.



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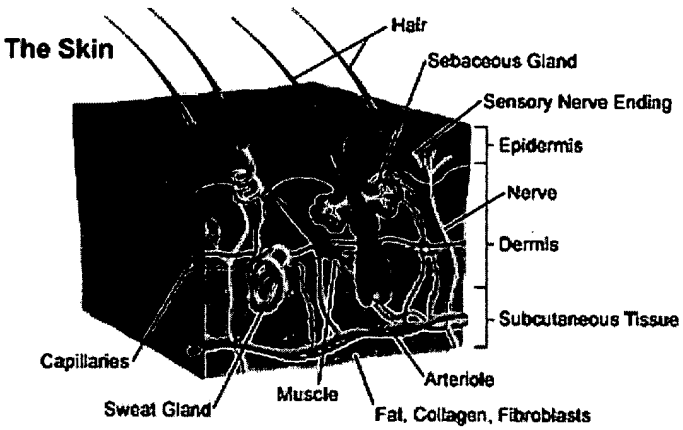
Anatomy of the Skin



Facts about the skin:

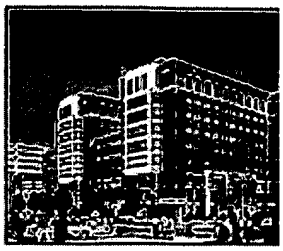
The skin is the body's largest organ, covering the entire body. In addition to serving as a protective shield against heat, light, injury, and infection, the skin also:

- regulates body temperature.
- stores water and fat.
- is a sensory organ.
- prevents water loss.
- prevents entry of bacteria.

Throughout the body, the skin's characteristics (thickness, color, texture) vary. For instance, the head contains more hair follicles than anywhere else, while the soles of the feet contain none. In addition, the soles of the feet and the palms of the hands are much thicker. The skin is made up of the following layers, with each layer performing specific functions:

- epidermis
- dermis
- subcutaneous fat layer

epidermis	The epidermis is the thin outer layer of the skin and consists of three parts: • **stratum corneum (horny layer)** This layer consists of fully mature



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	keratinocytes which contain fibrous proteins (keratins). The outermost layer is continuously shed. The stratum corneum prevents the entry of most foreign substances as well as the loss of fluid from the body. • **keratinocytes (squamous cells)** This layer, just beneath the stratum corneum, contains living keratinocytes (squamous cells), which mature and form the stratum corneum. • **basal layer** The basal layer is the deepest layer of the epidermis, containing basal cells. Basal cells continually divide, forming new keratinocytes that replace the cells that are shed from the skin's surface. The epidermis also contains melanocytes, which are cells that produce **melanin** (skin pigment).
dermis	The **dermis** is the middle layer of the skin. The dermis contains the following: • blood vessels • lymph vessels • hair follicles • sweat glands • collagen bundles • fibroblasts • nerves The dermis is held together by a protein called **collagen**, made by fibroblasts. This layer also contains pain and touch receptors.
subcutis	The **subcutis** is the deepest layer of skin. The subcutis, consisting of a network of collagen and fat cells, helps conserve the body's heat and protects the body from injury by acting as a shock absorber.

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2. Right mandibular posterior teeth
3. Left mandibular posterior teeth
4. Maxillary anterior teeth
5. Right maxillary posterior teeth
6. Left maxillary posterior teeth

Starting with the mandibular anterior teeth, examine the facial and proximal surfaces. Then, scale those surfaces. Next, examine and scale the lingual and proximal surfaces. After you have completed the mandibular anterior teeth, follow the routine until the entire dentition (all teeth) has been examined and scaled.

CALCULUS REMOVAL

Dental Technicians are only allowed to remove **supragingival calculus.** Supragingival calculus is defined as calculus **above the gumline.** Subgingival calculus removal and root planing are only to be performed by a dentist or dental hygienist. Figure 3-21 illustrates subgingival and supragingival calculus.

Scaling the teeth removes calculus by mechanically fracturing the deposits off each tooth. It is relatively simple to remove large deposits of supragingival calculus, but removing the smaller pieces that are left behind when the larger pieces fracture off takes practice to ensure the tooth surface is calculus-free.

Supragingival calculus may be detected visually. It will appear as a white, chalky, or yellow deposit on the tooth surface. Drying the tooth surface with air from the three-way syringe will make a deposit easier to see.

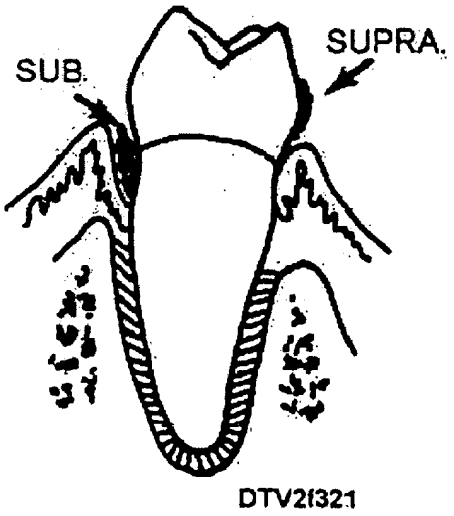

Figure 3-21.—Subgingival and supragingival calculus.

You can also detect supragingival calculus by passing the point of an explorer over the teeth. Enamel will feel hard and smooth as the explorer tip passes freely over it. Calculus feels rough and will interfere with the free movement of the explorer tip. The easiest way to detect supragingival calculus is by using a disclosing agent. This will enable you to visually identify stained areas of plaque and calculus.

SCALING INSTRUMENTS

Your choice of an instrument is determined primarily by the amount of calculus present. If the patient has a large amount of supragingival calculus or heavy stain, you may want to start your scaling procedure with the ultrasonic or sonic instrument. After you have removed the calculus or heavy stain, you then can use the various hand instruments to remove the remaining deposits. If the patient has a light to moderate accumulation of supragingival calculus, you may choose to complete the entire procedure with hand instruments.

INSTRUMENTATION

After you have located the calculus deposits, you are ready to perform the instrumentation necessary to remove them. There are four basic scaling strokes: exploratory, vertical, horizontal, and oblique.

Exploratory Stroke

The exploratory stroke is used to determine the general outline of the deposits. To perform the exploratory stroke, hold the scaler or curette lightly in a modified pen grasp. Holding the instrument lightly will increase your sense of touch. Establish a finger rest, then move the cutting edge of the blade across the tooth surface toward the gingiva. When you feel the calculus, continue moving the blade until the cutting edge reaches the border of the deposit. **Do not** insert the blade below the gingiva. Position the cutting edge of the instrument next to the border of the calculus deposit (fig. 3-22). You are now ready to change to a vertical, horizontal, or oblique scaling or working stroke (fig. 3-23) depending on the location of the calculus.

Vertical Stroke

The vertical stroke parallels the long axis of the tooth. Use this stroke to remove calculus from the proximal surfaces of the teeth. It is considered the

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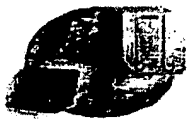

This course addresses the following subjects: dental radiology and examinations; preventive and operative dentistry; oral surgery; periodontal, endodontic, and prosthodontic assistance; dental treatment room emergencies, and forensic dentistry.

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USE: As cationic detergent and antiseptic; as laboratory reagent.

THERAP CAT: Topical antiseptic.

THERAP CAT (VET): Antiseptic, cleansing agent.

1982. Cetrimonium Stearate. *N,N,N-Trimethyl-1-hexadecanaminium octadecanoate; hexadecyltrimethylammonium stearate;* cetyltrimethylammonium stearate; trimethylhexadecylammonium stearate; Arquad 16 stearate; Dynafac. $C_{37}H_{77}NO_2$; mol wt 568.04. C 78.24%, H 13.66%, N 2.47%, O 5.63%. $[CH_3(CH_2)_{16}COO][CH_3(CH_2)_{15}N(CH_3)_3]$. Prepn: Gautier *et al., Bull. Soc. Chim. France* **1955**, 634.

Solid, mp 142-143°. Practically insol in water, alcohol.

Note: The commercial product, a waxy solid, also contains other alkyltrimethylammonium stearates, since the hexadecyl chain is derived from soybean fatty acids.

1983. Cetyl Alcohol. *1-Hexadecanol;* ethal; ethol; palmityl alcohol. $C_{16}H_{34}O$; mol wt 242.43. C 79.26%, H 14.14%, O 6.60%. $CH_3(CH_2)_{14}CH_2OH$. Discovered by Chevreul in 1813. Obtained from spermaceti by saponification: Spada, Gavioli, *Farm. Sci. e Tec.* (Pavia) **7**, 435 (1952), *C.A.* **47**, 891c (1953). Prepn from palmitoyl chloride + $NaBH_4$: Caikin, Brown, *J. Am. Chem. Soc.* **71**, 122 (1949); from methylthiopalmitate + Raney Ni: Ruzicka, Prelog, U.S. pat. **2,509,171** (1950 to Ciba); from hexadecyl bromide: Levine, Clippinger, U.S. pat. **3,018,308** (1962 to California Res. Corp.).

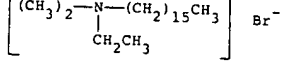
White crystals. d 0.811. mp 49°. bp 344°; bp_{15} 190°. n_D^{79} 1.4283. Practically insol in water; sol in alcohol, chloroform, ether.

Note: The *hexadecyl alcohol* developed by Esso Res. & Eng. Co. for cosmetics is a liquid, primary, branched chain, C_{16} alcohol, made up of an array of isomeric compds maintained in constant proportion by a complex manufacturing process (not from spermaceti): Edman, Lowden, *Drug Cosmet. Ind.* **93**, 631 (Nov. 1963). Liquid, d_{20}^{20} 0.842. bp_{50} 195-205°. Freezes at < −60°. Miscible with most alcohols, glycols, esters, ketones, cosmetic oils and aromatics. Immiscible with water.

USE: In cosmetics as emollient, emulsion modifier, coupling agent.

THERAP CAT: Pharmaceutic aid (emulsifying and stiffening agent).

1984. Cetyldimethylethylammonium Bromide. *N-Ethyl-N,N-dimethyl-1-hexadecanaminium bromide; ethylhexadecyldimethylammonium bromide;* ethyl cetab; CDA; Ammonyx DME; Bretol. $C_{20}H_{44}BrN$; mol wt 378.49. C 63.47%, H 11.72%, Br 21.11%, N 3.70%. Cationic germicidal detergent. Prepn and antibacterial activity: R. S. Shelton *et al., J. Am. Chem. Soc.* **68**, 753 (1946).



White powder, mp 178-186°. Sol in water, alcohol; slightly sol in chloroform, benzene, ether. LD_{50} orally in rats: 500 mg/kg, *RTECS* **Vol. 1**, R. J. Lewis, R. L.Tatken, Eds. (1979) p 107.

USE: Disinfectant; laboratory reagent.

THERAP CAT: Topical antiseptic.

THERAP CAT (VET): Topical antiseptic.

1985. Cetyl Lactate. *2-Hydroxypropanoic acid hexadecyl ester; 1-hexadecanol lactate;* lactic acid cetyl ester; lactic acid hexadecyl ester; Ceraphyl 28. $C_{19}H_{38}O_3$; mol wt 314.49. C 72.56%, H 12.18%, O 15.26%. $CH_3CHOHCOOC_{16}H_{33}$. Preparation: Rehberg, Marion, *J. Am. Chem. Soc.* **72**, 1918 (1950).

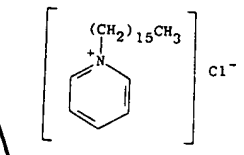
Waxy solid. mp 41°. $bp_{0.1}$ 132°; bp_1 170°; bp_{10} 219°. n_D^{40} 1.4410; n_D^{50} 1.4370.

USE: Non-ionic emollient. To improve feel and texture of cosmetic and pharmaceutical prepns.

1986. Cetyl Palmitate. *Hexadecanoic acid hexadecyl ester; palmitic acid hexadecyl ester;* hexadecyl palmitate. $C_{32}H_{64}O_2$; mol wt 480.83. C 79.93%, H 13.41%, O 6.65%. $CH_3(CH_2)_{14}COOCH_2(CH_2)_{14}CH_3$. Prepn from palmitoyl chloride and cetyl alcohol in the presence of Mg: Paquot, Bouquet, *Bull. Soc. Chim. France* **1947**, 321; by CrO_3-H_2SO_4 oxidation of cetyl alcohol: Cymerman-Craig, Horning, *J. Org. Chem.* **25**, 2098 (1960). Biosynthesis using inoculum of *Nocardia salmonicolor:* Davis, U.S. pat. **3,169,099** (1965 to Socony Mobil Oil).

Monoclinic leaflets, mp 54°. d^{20} 0.989. n_D^{70} 1.4398. Practically insol in water; sol in abs alc, ether.

1987. Cetylpyridinium Chloride. *1-Hexadecylpyridinium chloride;* Ceepryn; Cepacol; Cetamium; Dobendan; Medilave; Pristacin; Pyrisept. $C_{21}H_{38}ClN$; mol wt 339.99. C 74.19%, H 11.26%, Cl 10.43%, N 4.12%. Pharmacology and toxicology: *J. Pharmacol. Exp. Ther.* **74**, 401 (1942). Review of early literature: C. L. Huyck, *Am. J. Pharm.* **116**, 50 (1944).

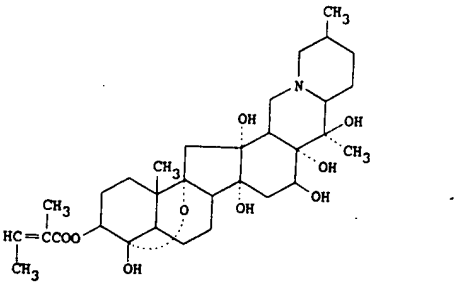


Monohydrate, white powder. mp 77-83°. Freely sol in water, alcohol, chloroform; very slightly sol in benzene, ether. pH (1% aq soln): 6.0 to 7.0. Surface tension (25°): 43 dyn/cm (0.1% aq soln); 41 dyn/cm (1.0%); 38 dyn/cm (10%). LD_{50} in rats (mg/kg): 250 s.c.; 6 i.p.; 30 i.v.; 200 orally, J. W. Nelson, S. C. Lyster, *J. Am. Pharm. Assoc.* **35**, 89 (1946).

THERAP CAT: Anti-infective, topical; pharmaceutic aid (preservative).

THERAP CAT (VET): Topical antiseptic, disinfectant.

1988. Cevadine. *(Z)-4α,9-Epoxycevane-3β,4,12,14,16β,17,20-heptol 3-(2-methyl-2-butenoate);* veratrine. $C_{32}H_{49}NO_9$; mol wt 591.72. C 64.95%, H 8.35%, N 2.37%, O 24.33%. From seeds of *Schoenocaulon officinale* (Schlecht & Cham.) A. Gray *(Sabadilla officinarum* Brandt), *Liliaceae:* Poetsch *et al., J. Am. Pharm. Assoc.* **38**, 525 (1949); Ringel, *ibid.* **45**, 433 (1956). Structure: Kupchan, Alfonso, *ibid.* **49**, 242 (1960). *Review:* Wintersteiner in Graff, *Essays in Biochemistry* (Wiley, New York, 1956) pp 308-321.



Flat needles from ether, decomp 213-214.5°. $[\alpha]_D^{20}$ +12.8° (c = 3.2 in alc). One gram dissolves in about 15 ml alc or ether; slightly sol in water. LD_{50} i.p. in mice: 3.5 mg/kg, Swiss, Bauer, *Proc. Soc. Exp. Biol. Med.* **76**, 847 (1951).

Aurichloride, fine yellow needles from alc, dec 190°.

Mercurichloride, $C_{32}H_{49}NO_9.HCl.HgCl_2$, silvery scales, dec 172°.

USE: Evaluation as insecticide: Ikawa, Link *et al., J. Biol. Chem.* **159**, 517 (1945). *Caution:* Extremely irritating locally, particularly to mucous membranes. Serious poisoning has resulted from local application. Caution must be used in handling. *See also* Veratrine (Mixture).

1989. Cevine. *4,9-Epoxycevane-3α,4β,12,14,16β,17,20-heptol.* $C_{27}H_{43}NO_8$; mol wt 509.65. C 63.63%, H 8.51%, N 2.74%, O 25.12%. By hydrolysis of cevadine. Structure and stereochemistry: Barton *et al., Experientia* **10**, 81 (1954); Kupchan *et al., J. Am. Chem. Soc.* **80**, 1769 (1958); Kupchan

in mice, rats: 23±0.7, 21.5±1.8 mg/kg, L. Orö, A. Wretlind, *Acta Pharmacol. Toxicol.* **18**, 141 (1961).

U.S.P. stearic acid consists chiefly of a mixture of stearic and palmitic acids. It is in the form of white or slightly yellow, crystal masses, or a white to slightly yellow powder; slight tallow-like odor. Does not congeal below 54°.

Ethyl ester, $C_{20}H_{40}O_2$, *ethyl stearate.* White, cryst solid; odorless or practically so. mp 33-35°. bp 224°. Ethyl stearate of commerce solidifies at 20-24°; bp_4 180°. Insol in water; sol in alcohol or ether.

Methyl ester, $C_{19}H_{38}O_2$, *methyl stearate.* White crystals. mp 38-39°. bp_{15} 215°. Insol in water; sol in alcohol, ether.

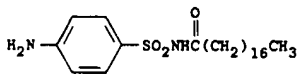
USE: For suppositories, coating enteric pills, ointments, and for coating bitter remedies. Manuf stearates of aluminum, zinc, and other metals, stearin soap for opodeldoc, candles, phonograph records, insulators, modeling compds; impregnating plaster of Paris; in vanishing creams and other cosmetics.

8655. Stearyl Alcohol. *1-Octadecanol;* stenol. $C_{18}H_{38}O$; mol wt 270.48. C 79.92%, H 14.16%, O 5.91%. $CH_3(CH_2)_{16}CH_2OH$. The official substance is a mixture of solid alcohols consisting chiefly of stearyl alcohol. Preparation from ethyl stearate: Brown, Rao, *J. Am. Chem. Soc.* **78**, 2582 (1956); Hesse, Schrödel, *Ann.* **607**, 24 (1954). Prepn of technical grade from sperm whale oil: Maiorov *et al., Zh. Prikl. Khim.* **37**, 1344 (1964).

Unctuous white flakes or granules, mp 56-60° (the pure substance, mp 59.4-59.8°, bp_{15} 210°). Sol in alcohol, ether, benzene, acetone.

USE: Substitute for cetyl alc in pharmaceutical dispensing, in cosmetic creams, for emulsions, textile oils and finishes, as antifoam agent, lubricant, and chemical raw material.

8656. Stearylsulfamide. *N-[(4-Aminophenyl)sulfonyl]-octadecanamide; N-sulfanilylstearamide; N¹*-stearoylsulfanilamide; *N¹*-octadecanoylsulfanilamide; Keralba. $C_{24}H_{42}N_2O_3S$; mol wt 438.66. C 65.71%, H 9.65%, N 6.39%, O 10.94%, S 7.31%. Prepn: Crossley *et al., J. Am. Chem. Soc.* **61**, 2930 (1939); Hultquist, Northey, U.S. pat. **2,456,051** (1948 to Am. Cyanamid).

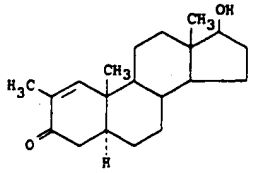


Irregular plates from 70% alc, mp 98-102°.

THERAP CAT: Dermatologic.

8657. Steffen's Waste. Steffen's filtrate. Waste water, rich in sodium glutamate, from the Steffen lime process of obtaining sugar from sugar beets.

8658. Stenbolone. *17β-Hydroxy-2-methyl-5α-androst-1-en-3-one;* 2-methyl-5α-androst-1-en-17β-ol-3-one; 2-methyl-17β-hydroxy-5α-androst-1-en-3-one; stenobolone (rescinded USAN). $C_{20}H_{30}O_2$; mol wt 302.44. C 79.42%, H 10.00%, O 10.58%. Preparation of free alcohol and acetate: Mauli, *J. Am. Chem. Soc.* **82**, 5494 (1960); Kaspar *et al.*, Ger. pat. **1,096,356** (1961 to Schering AG), *C.A.* **55**, 27440b (1961); Counsell *et al., J. Org. Chem.* **27**, 248 (1962); Brit. pat. **925,849** (1963 to Syntex).



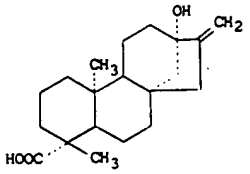
Crystals from acetone + hexane, mp 155-158°. $[\alpha]_D$ +52° (chloroform), $[\alpha]_D^{26}$ +47° (chloroform). uv max (95% ethanol): 241 nm (log ε 3.99).

Acetate, $C_{22}H_{32}O_3$, *Anatrofin.* Crystals from acetone + hexane, mp 146-149°. $[\alpha]_D$ +32° (chloroform), $[\alpha]_D^{26}$ +60° (chloroform): *see* Mauli *et al.*, and Counsell *et al.* uv max (95% ethanol): 241 nm (log ε 4.03).

THERAP CAT: Acetate as anabolic.

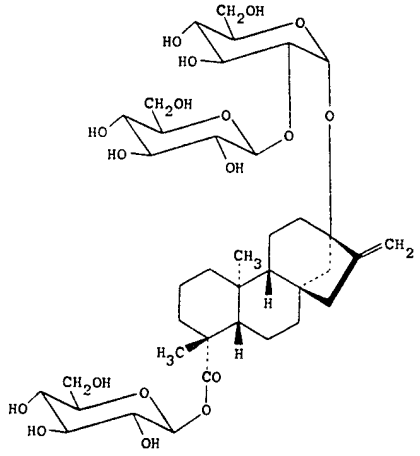
8659. Stephanite. $5Ag_2S.Sb_2S_3$—silver antimony sulfide.

8660. Steviol. *13-Hydroxykaur-16-en-18-oic acid;* hydroxydehydrostevic acid. $C_{20}H_{30}O_3$; mol wt 318.44. C 75.43%, H 9.50%, O 15.07%. Aglucon of stevioside, the sweet glucoside abundant in leaves and stems of *Stevia rebaudiana* Bert. Prepn by enzymatic hydrolysis of stevioside: Mosettig, Nes, *J. Org. Chem.* **20**, 884 (1955). Structure and stereochemistry: Dolder *et al., J. Am. Chem. Soc.* **82**, 246 (1960); Vorbrueggen, Djerassi, *ibid.* **84**, 2990 (1962). Absolute configuration: Mosettig *et al., ibid.* **85**, 2305 (1963). Biosynthesis: Ruddat *et al., Arch. Biochem. Biophys.* **110**, 496 (1965). Total synthesis of *dl*-form: Mori *et al., Tetrahedron Letters* **1970**, 2411; Cook, Knox, *ibid.* 4091; *eidem, Tetrahedron* **28**, 3217 (1972).



Needles from methanol or ethanol + water, mp 215°. $[\alpha]_D$ −94.7°.

8661. Stevioside. *13-[(2-O-β-D-Glucopyranosyl-α-D-glucopyranosyl)oxy]kaur-16-en-18-oic acid β-D-glucopyranosyl ester;* steviosin. $C_{38}H_{60}O_{18}$; mol wt 804.90. C 56.70%, H 7.51%, O 35.78%. Isolated from leaves of *Stevia rebaudiana* (Bert.) Hemsl. (*Eupatorium rebaudianum* Bert.), *Compositae,* also called *yerba dulce. Habit.* Paraguay. Review of botany: Samaniego, *Rev. farm. (Buenos Aires)* **88**, 199 (1946). Review of chemistry and use as sweetening agent: Bell, *Chem. & Ind. (London)* **1954**, 897; Fletcher, Jr., *Chemurgic Digest* **14**, 7, 18 (July-Aug. 1955); *Chem. & Eng. News* **34**, 124 (1956). Isoln and structure: Wood *et al., J. Org. Chem.* **20**, 875 (1955). Additional structure work: Vis, Fletcher, *J. Am. Chem. Soc.* **78**, 4709 (1956); Dolder *et al., ibid.* **82**, 246 (1960). Partial synthesis: T. Ogawa *et al., Carbohyd. Res.* **60**, C7 (1978). Total synthesis: *eidem, Tetrahedron* **36**, 2641 (1980). Synthesis and sensory evaluation of analogues: G. E. Dubois *et al., J. Med. Chem.* **24**, 1269 (1981).

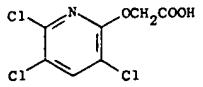


Hygroscopic crystals, mp 198°; $[\alpha]_D^{25}$ −39.3° (c = 5.7 in H_2O); 300 times as sweet as cane sugar. One gram dissolves in 800 ml water. Sol in dioxane. Slightly sol in alc.

USE: Has been proposed as non-nutritive sweetening agent.

8662. Stibamine Glucoside. Sodium *p*-aminobenzenestibonate glucoside; sodium stibanilate glucoside; glucostibamine sodium; glucostimidine sodium; Neostam. $C_{36}H_{49}N_3NaO_{22}Sb_3$; mol wt 1264.05. C 34.20%, H 3.91%, N 3.32%,

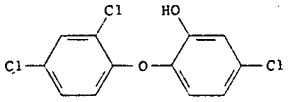
3,862,952 (1975 to Dow). Activity: B. C. Byrd *et al., Proc. South. Weed Sci. Soc.* **28**, 251 (1975).



Fluffy solid, mp 148-150°. Vapor press at 25°: 1.26 × 10^{-6} mm Hg. pKa 2.68. Subject to photolysis. Soly in water at 25°: 440 mg/l. Soly at 25° (g/kg): acetone 989; 1-octanol 307. LD_{50} orally in rats: 713 mg/kg, *RTECS* Vol. I, R. J. Lewis, R. L. Tatken, Eds. (1979) p 39.

USE: Herbicide.

9471. Triclosan. *5-Chloro-2-(2,4-dichlorophenoxy)phenol;* 2,4,4'-trichloro-2'-hydroxydiphenyl ether; CH 3635 (formerly); Irgasan CH 3635 (formerly); Irgasan DP 300. $C_{12}H_7Cl_3O_2$; mol wt 289.53. C 49.78%, H 2.44%, Cl 36.73%, O 11.05%. Prepn: Neth. pat. **Appl. 6,401,526** corresp to E. Model, J. Bindler, U.S. pat. **3,506,720** (1964, 1970 to Geigy). Physical and bacteriostatic properties: C. A. Savage, *Drug Cosmet. Ind.* **109**(3), 36, 161 (1971). Metabolism: J. G. Black *et al., Toxicology* **3**, 33 (1975). Toxicology: F. L. Lyman, T. Furia, *Ind. Med. Surg.* **38**(2), 64 (1969), *C.A.* **71**, 89601h (1969).

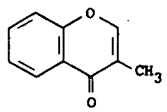


White to off-white crystalline powder, slight, faintly aromatic odor. mp 54-57.3°. Vapor press. (20°C) 4 × 10^{-6} mm Hg. pKa 7.9. Insol in water; readily sol in alkaline solns and many organic solvents.

USE: Bacteriostat and preservative for cosmetic and detergent prepns: E. Model, J. Bindler, U.S. pat. **3,629,477** (1971 to Geigy).

THERAP CAT: Disinfectant.

9472. Tricromyl. *3-Methyl-4H-1-benzopyran-4-one; 3-methylchromone;* 3-methyl-γ-benzopyrone; Crodimyl; Cromonalgina; Spasmocromona. $C_{10}H_8O_2$; mol wt 160.16. C 74.99%, H 5.03%, O 19.98%. Based on an ancient Egyptian drug now termed *bezr el khelda.* Prepn from *o*-hydroxypropiophenone: Clerc-Bory *et al., Bull. Soc. Chim. France* **1955**, 1083; Mentzer, Meunier, Fr. pat. **980,785** (1951 to Lab. Franc. Chimiother.); Mentzer, U.S. pat. **2,769,015** (1956 one-half to Laroche-Navarron).



Crystals from ethanol, mp 68°. uv max (alc): 304 nm.

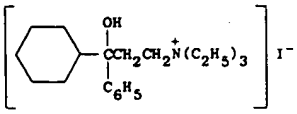
THERAP CAT: Antispasmodic; coronary vasodilator.

9473. Tridecylbenzene. *1-Phenyltridecane;* Detergent Alkylate #5; Tridane. $C_{19}H_{32}$; mol wt 260.45. C 87.62%, H 12.38%. $C_6H_5(CH_2)_{12}CH_3$. Prepn: Ziegler *et al., Ann.* **511**, 13 (1934). Manufacture: Williamson, Bieneman, U.S. pat. **3,207,800** (1965 to Continental Oil).

Liquid, bp 346°, bp_{10} 188-189.5°. fp 10°. d_4^{20} 0.8550, d_4^{25} 1.8515. n_D^{20} 1.4821, n_D^{25} 1.4800. Forms stable foams in the presence of fat.

USE: In manuf of detergents and surface-active agents. Can be sulfonated.

9474. Tridihexethyl Iodide. *γ-Cyclohexyl-N,N,N-triethyl-γ-hydroxybenzenepropanaminium iodide; (3-cyclohexyl-3-hydroxy-3-phenylpropyl)triethylammonium iodide;* 3-diethylamino-1-cyclohexyl-1-phenyl-1-propanol ethiodide; 3-diethylamino-1-phenyl-1-cyclohexyl-1-propanol ethiodide; α-(2-diethylaminoethyl)-α-phenylcyclohexanemethanol ethiodide; propethonum iodide; tridihexethide; 921 C; Claviton. $C_{21}H_{36}INO$; mol wt 445.44. C 56.63%, H 8.15%, I 28.49%, N 3.14%, O 3.59%. Prepn: Lobby, U.S. pat. **2,913,494** (1959 to Am. Cyanamid).

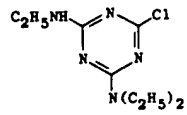


Bitter crystals, mp 179-184°. Solubility in water at 25°: 1.1 g/100 ml. Freely sol in alc, chloroform. Very slightly sol in ether. pH of a 1% aq soln 5.5-7.

Note: The name *Pathilon* previously used for the iodide is now used for *tridihexethyl chloride.*

THERAP CAT: Anticholinergic.

9475. Trietazine. *6-Chloro-N,N,N'-triethyl-1,3,5-triazine-2,4-diamine; 2-chloro-4-diethylamino-6-ethylamino-s-triazine;* 2-ethylamino-4-diethylamino-6-chloro-*s*-triazine. G 27901; NC 1667; Gesafloc. $C_9H_{16}ClN_5$; mol wt 229.73. C 47.06%, H 7.02%, Cl 15.44%, N 30.49%. Prepn: Pearlman, Banks, *J. Am. Chem. Soc.* **70**, 3726 (1948).



Crystals from propanol, mp 100-102°. Soly at 25°: 20 ppm in water; 17% in acetone; 20% in benzene; > 50% in chloroform; 10% in dioxane; 3% in ethanol. LD_{50} orally in rats: 1750 mg/kg, G. W. Bailey, J. L. White, *Residue Rev.* **10**, 97 (1965).

USE: Herbicide.

9476. Triethanolamine. *2,2',2''-Nitrilotriethanol;* trihydroxytriethylamine; tris(hydroxyethyl)amine; triethylolamine. $C_6H_{15}NO_3$; mol wt 149.19. C 48.30%, H 10.13%, N 9.39%, O 32.17%. $N(CH_2CH_2OH)_3$. Produced along with mono- and diethanolamine by ammonolysis of ethylene oxide. *See the refs under* Ethanolamine. Monograph: E. J. Fischer, *Triäthanolamin und andere Alkanolamine* (Heidelberg, 4th ed., 1954).

Very hygroscopic, viscous liq. Slight ammoniacal odor. Turns brown on exposure to air and light. d_4^{20} 1.1242; d_4^{60} 1.0985. One gallon weighs 9.37 lbs. fp 21.57°; bp_{760} 335.4°. McDonald *et al., J. Chem. Eng. Data* **4**, 311 (1959). Viscosity (centipoise) at 25°: 590.5; viscosity at 60°: 65.7. Strong base. K at 25° = 3.15 × 10^{-10}. pH of 0.1 *N* aq soln 10.5. n_D^{20} 1.4852. Flash pt 365°F. Miscible with water, methanol, acetone. Soly at 25° in benzene, 4.2%; in ether, 1.6%; in carbon tetrachloride, 0.4%; in *n*-heptane, < 0.1%.

Hydrochloride, crystals from ethanol, mp 177°.

Salicylate, *Mobisyl, Myoflex.*

USE: Intermediate in the manuf of surface active agents, textile specialties, waxes, polishes, herbicides, petroleum demulsifiers, toilet goods, cement additives, cutting oils. In making emulsions with mineral and vegetable oils, paraffin and waxes. Solvent for casein, shellac, dyes; manuf synthetic resins; increasing the penetration of organic liquids into wood and paper. In the production of lubricants for the textile industry.

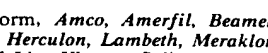
THERAP CAT: Pharmaceutic aid (alkalizing agent).

9477. Triethylamine. *N,N-Diethylethanamine.* $C_6H_{15}N$; mol wt 101.19. C 71.21%, H 14.94%, N 13.84%. $(C_2H_5)_3N$. Prepd by reaction of *N,N*-diethylacetamide with lithium aluminum hydride: Uffer, Schlittler, *Helv. Chim. Acta* **31**, 1397 (1948). Manuf by vapor phase alkylation of ammonia with ethanol: Lemon, Myerly, U.S. pat. **3,022,349** (1962 to Union Carbide).

Liquid; strong ammoniacal odor; d_4^{25} 0.7255; mp −115°; bp 89-90°; n_D^{20} 1.4003. Flash pt, closed cup: 20°F (−6°C). Slightly sol in water above 18.7°; misc with alcohol, ether, also with water below 18.7°. *Keep well closed.* LD_{50} orally in rats: 0.46 g/kg, H. F. Smyth *et al., Arch. Ind. Hyg. Occup. Med.* **4**, 119 (1951).

Hydrochloride, $C_6H_{15}N.HCl$, crystals from alcohol; mp

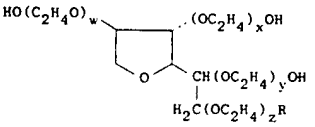
mer. Three forms are possible. *Isotactic* (fiber-forming): methyl groups are all on same side of plane of zig-zag carbon atom chain. *Syndiotactic:* methyl groups are on alternate sides of plane of carbon atom chain. *Atactic* (not fiber-forming, amorphous): methyl groups are in a random arrangement with respect to plane of carbon atom chain. Early synthesis of isotactic form with Ziegler catalyst and comparison with atactic form: Natta *et al., J. Chem. Soc.* 77, 1708 (1955); Natta, *J. Polymer Sci.* 16, 143 (1955). *Reviews:* N. G. Gaylord, H. F. Mark, *Linear and Stereoregular Addition Polymers* (Interscience, New York, 1959) pp 54-65; R. W. Moncrieff, *Man-Made Fibres* (Wiley, NewYork, 4th ed., 1963) pp 500-510; J. G. Cook, *Handbook of Textile Fibres* (Merrow Publishing Co., England, 3rd ed., 1964) pp 369-379; B. C. Repka, Jr. in Kirk-Othmer *Encyclopedia of Chemical Technology* Vol. 14 (Wiley-Interscience, New York, 2nd ed., 1967) pp 282-309.



Isotactic form, ***Amco, Amerfil, Beamette, Courlene PY, DLP, Gerfil, Herculon, Lambeth, Meraklon, Moplen, Olane, Prolene, Tuff-Lite, Ulstron.*** Solid material, softens at about 155°, mp at about 165°. Low flammability comparable to that of wool. Keeps strength down to −100°. Specific gravity 0.90-0.92. Practically insol in cold org solvents; sol in hot decalin, hot tetralin, boiling tetrachloroethane. Shrinks in boiling trichloroethylene. Resistant to acids, alkalies; attacked by strong oxidizing agents, *e.g.*, hydrogen peroxide. Good resistance to abrasion ("pilling"). Tendency to develop static charges. Unstabilized material has poor resistance to sunlight. Difficult to dye, lacks dye-attracting polar groups in structure.

USE: Isotactic form: for fishing gear, ropes, filter cloths, laundry bags, protective clothing, blankets, fabrics, carpets, yarns, etc.

7455. Polysorbate 80. *Sorbitan mono-9-octadecenoate poly(oxy-1,2-ethanediyl) derivs;* polyoxyethylene (20) sorbitan mono-oleate; sorethytan (20) mono-oleate; polyethylene oxide sorbitan mono-oleate; Sorbitan mono-oleate polyoxyethylene; Sorlate; Tween 80; Monitan; Olothorb. An oleate ester of sorbitol and its anhydrides copolymerized with approx 20 moles of ethylene oxide for each mole of sorbitol and sorbitol anhydrides. *See also* Span.



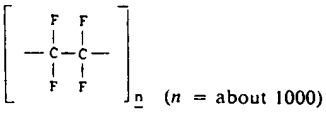
[Sum of w, x, y, z is 20; R is $(C_{17}H_{33})COO$]

Amber-colored, viscous liquid. d 1.06-1.10. Viscosity 270-430 centistokes. Very sol in water; sol in alcohol, cottonseed oil, corn oil, ethyl acetate, methanol, toluene. Insol in mineral oil. pH of 5% aq soln between 5 and 7.

USE: The U.S.P. grade is used as emulsifier and dispersing agent for medicinal products designed for internal use. As defoamer and emulsifier in foods.

THERAP CAT: Pharmaceutic aid (surfactant).

7456. Polytef. *Tetrafluoroethene homopolymer; tetrafluoroethylene polymer;* polytetrafluoroethylene resin; Teflon; Fluon; Fluoroflex. A plastic tetrafluoroethylene homopolymer. Composed of very long chains of linked CF_2 units. Prepd by polymerization of tetrafluoroethylene: Plunkett, U.S. pat. 2,230,654 (1941 to Kinetic Chem.); Brubaker, U.S. pat. 2,393,967 (1946 to du Pont); Joyce, U.S. pat. 2,394,243 (1946 to du Pont); Hanford, Joyce, *J. Am. Chem. Soc.* 68, 2082 (1946); Renfrew, Lewis, *Ind. Eng. Chem.* 38, 870 (1946); Renfrew, U.S. pat. 2,534,058 (1950 to du Pont); C. E. Schildknecht, *Vinyl and Related Polymers* (Wiley, New York, 1952) pp 483-494. Story of discovery by Roy J. Plunkett during summer of 1938: *J. Chem. Ed.* 39, 288 (1962). *Reviews:* R. W. Moncrieff, *Man-Made Fibres* (John Wiley, New York, 4th ed.,. 1963) pp 512-517; McCane in *Encyclopedia of Polymer Science and Technology* vol. 13, N. M. Bikales, Ed. (Interscience, New York, 1970) pp 623-654.



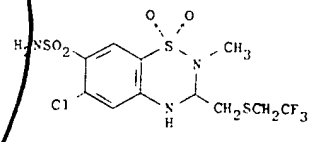
(*n* = about 1000)

Non-flammable, tough plastic. Grayish white transparent thin sheets. Very inert chemically. Useful temp range −75° to +250°. Gels at 325° and at 400° reverts to the gaseous monomer. d 2.25. Shore hardness 55-56. Tensile strength 3500-4500 psi. Flexural strength 2000 psi. Brittle point below −80°. Dielectric constant (at 60 to 3 × 10^9 cycles) 2.0-2.05. Not affected by water, aqua regia, chlorosulfonic acid, acetyl chloride, boron fluoride, hot nitric acid, boiling solns of sodium hydroxide, and organic solvents. Not wetted by water. No substance has been found which will dissolve the polymer, but prolonged contact with fluorine, hot plasticizers and polymeric waxes is not recommended. Deteriorates with age and is subject to cold flow at high pressure. Cannot be molded, but can be extruded and pressed into shapes at around 205°. Does not stick to anything.

USE: As tubing and sheets for chemical laboratory and process work; for lining reaction vessels; for gaskets and pump packings, sometimes mixed with graphite; as electrical insulator esp in high frequency applications; filtration fabrics; protective clothing. *Caution:* The finished compd is inert under ordinary conditions. There have been reports of polymer fume fever in humans exposed to unfinished product. Pyrolysis products are irritating to mucous membrane.

THERAP CAT: Prosthetic aid.

7457. Polythiazide. *6-Chloro-3,4-dihydro-2-methyl-3-[[(2,2,2-trifluoroethyl)thio]methyl]-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide;* 2-methyl-3-(β,β,β-trifluoroethylthiomethyl)-6-chloro-7-sulfamyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide; 6-chloro-3,4-dihydro-2-methyl-7-sulphamoyl-3-(2,2,2-trifluoroethylthiomethyl)-2*H*-benzo-1,2,4-thiadiazine 1,1-dioxide; Drenusil; Nephril; Renese. $C_{11}H_{13}ClF_3N_3O_4S_3$; mol wt 439.90. C 30.03%, H 2.98%, Cl 8.06%, F 12.96%, N 9.55%, O 14.55%, S 21.87%. Prepn: McManus, U.S. pat. 3,009,911 (1961 to Pfizer).



Crystals from isopropanol, mp 202.5°. Practically insol in water. Sol in aq solns made alkaline with carbonates or hydroxides of the alkali metals. Rate of decompn increases with increase in pH.

THERAP CAT: Diuretic, antihypertensive.

7458. Polyvinyl Alcohol. *Ethenol homopolymer;* PVA; Alvyl; Elvanol; Gelvatol; Moviol; Polyviol; Resistoflex; Rhodoviol; Solvar; Vinarol; Vinol. A polymer prepd from polyvinyl acetates by replacement of the acetate groups with hydroxyl groups. The alcoholysis proceeds most rapidly in a methanol + methyl acetate mixture in the presence of catalytic amounts of alkali or mineral acids: Hermann, Haehnel, *Ber.* 60, 1658 (1927). *Monograph:* C. E. Schildknecht, *Vinyl and Related Polymers* (Wiley, New York, 1952). The head-to-tail or 1,3-glycol structure is favored: Staudinger *et al., Ber.* 60, 1782 (1927); *J. Prakt. Chem.* 155, 261 (1940); Marvel, Denoon, *J. Am. Chem. Soc.* 60, 1045 (1938); McDowell, Kenyon, *ibid.* 62, 415 (1940); Marvel, Inskeep, *ibid.* 65, 1710 (1943). *Reviews:* M. Leeds in Kirk-Othmer *Encyclopedia of Chemical Technology* vol. 21 (Wiley-Interscience, New York, 2nd ed., 1970) pp 353-368; *Polyvinyl Alcohol.* A. C. Finch, Ed. (Wiley, New York, 1973) 640 pp; A. S. Dunn, *Chem. &*

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THE MERCK INDEX

TENTH EDITION

butyl alcohol, [NF] a clear, colorless, mobile liquid, C_4H_9OH, with a characteristic odor, occurring in four isomeric forms; used as a solvent.

cetostearyl alcohol, [NF] a mixture of stearyl alcohol and cetyl alcohol, used as an emulsifier; the official preparation consists of at least 40 per cent stearyl alcohol and at least 90 per cent of stearyl and cetyl alcohols combined.

cetyl alcohol, [NF] a solid fatty alcohol prepared by hydrogenation of palmitic acid or by saponification of spermaceti, used as an emulsifying and stiffening agent; the official preparation contains not less than 90 per cent cetyl alcohol, with the remainder consisting mainly of related alcohols.

dehydrated alcohol, [USP] an extremely hygroscopic, transparent, colorless, volatile liquid with characteristic odor and burning taste, containing at least 99.5 per cent ethanol by volume; used as a solvent and administered by injection into nerves and ganglia for relief of pain. Called also *absolute a.*

denatured alcohol, ethanol which has been rendered unfit for internal use by addition of an adulterant such as methanol or acetone, but which may still be used for other purposes including industrial processes, as a solvent, on the skin as a cooling agent, and as a skin disinfectant.

dihydric alcohol, an alcohol containing two hydroxyl groups.

diluted alcohol, [NF] a mixture of alcohol and water, used as a solvent; the official preparation contains 41 to 42 per cent ethanol by weight, or 48.4 to 49.5 per cent by volume, at 15.56° C.

ethyl alcohol, ethanol.

fatty alcohol, any of a group of high molecular weight primary alcohols, usually straight chain; they may be synthetic or derived from natural oils and are used in pharmacy and as solvents, detergents, and emulsifiers.

glyceryl alcohol, **glycyl alcohol**, glycerin.

grain alcohol, ethanol.

isoamyl alcohol, one of the isomeric forms of amyl alcohol; used as a solvent and in pharmacy.

isopropyl alcohol, [USP] an isomer of propyl alcohol and a homologue of ethyl alcohol, having disinfectant properties similar to those of ethyl alcohol; used as a solvent and disinfectant and applied topically as an antiseptic. Called also *dimethyl carbinol* and *isopropanol.*

isopropyl rubbing alcohol, [USP] a preparation containing 68–72 per cent isopropyl alcohol in water, used as a rubefacient.

lanolin alcohols, [NF] a mixture of aliphatic alcohols, triterpenoid alcohols, and sterols, obtained by hydrolysis of lanolin; used as an emulsifying agent in the preparation of water-in-oil emulsions. Called also *wool a's.*

methyl alcohol, methanol.

monohydric alcohol, an alcohol containing only one hydroxyl group.

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A

alcohol — algaroba

alcohol (al co hol) (al'k[schwa]-hol) [Arabic *al kuhl* fine powder of antimony or other distilled substance] [USP] 1. any of a class of organic compounds formed from the hydrocarbons by substitution of one or more hydroxyl groups for an equal number of hydrogen atoms; the term is extended to various substitution products that are neutral in reaction and that contain one or more of the alcohol groups. 2. ethanol. 3. the official preparation of ethanol, containing not less than 92.3 per cent and not more than 93.8 per cent of ethanol by weight.

absolute alcohol, dehydrated a.

amyl alcohol, a colorless oily liquid, $C_5H_{11}OH$, with characteristic odor, occurring as several isomers; miscible with alcohol, ether, and chloroform and slightly soluble in water, and used as solvents and in pharmaceutical preparations.

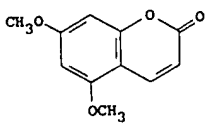
amyl alcohol, tertiary, amylene hydrate.

aromatic alcohol, an aromatic compound in which the side chain on the benzene ring contains a hydroxyl group; e.g., phenol.

azeotropic isopropyl alcohol, [USP] a preparation containing 91–93 per cent isopropyl alcohol by volume and water.

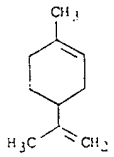
benzyl alcohol, [NF] a clear colorless oily liquid occurring in balsam of Peru, tolu balsam, and styrax; used as a bacteriostatic in solutions for injection and topically as a local anesthetic. Called also *benzenemethanol, phenylcarbinol* and *phenylmethanol.*

of *Citrus lima* Lunan (*C. limetta* Auth.), *Rutaceae* (lime): Tilden, Beck, *J. Chem. Soc.* **57**, 323 (1890); from W. Indian lime oil: Caldwell, Jones, *ibid.* **1945**, 570; from citrus oils: Stanley, Vannier, U.S. pat. **2,889,337** (1959 to U.S.D.A.). Synthesis: Schmidt, *Arch. Pharm.* **242**, 288 (1904); Heyes, Robertson, *J. Chem. Soc.* **1936**, 1831.



Needles from methanol, mp 147-148°. uv max (alcohol): 222, 247, 250.5, 324 nm (log ε 4.03, 3.84, 3.84, 4.18). Almost insol in boiling water, ether, petr ether; freely sol in alcohol, chloroform, acetone.

5321. Limonene. *1-Methyl-4-(1-methylethenyl)cyclohexene; p-mentha-1,8-diene;* cinene; cajeputene; kautschin. $C_{10}H_{16}$; mol wt 136.23. C 88.16%, H 11.84%. Occurs in various ethereal oils, particularly in oils of lemon, orange, caraway, dill and bergamot. Isoln of *d*-limonene from mandarin peel oil *(Citrus reticulata* Blanco, *Rutaceae):* Kugler, Kováts, *Helv. Chim. Acta* **46**, 1480 (1963). *Review:* J. L. Simonsen, *The Terpenes* vol. I (University Press, Cambridge, 2nd ed., 1947) pp 143-165.



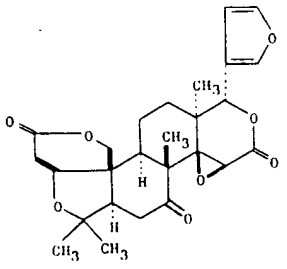
dl-Form, *inactive limonene, dipentene.* Liquid. Pleasant lemon-like odor. bp_{763} 175.5-176.5°. $d_4^{20.85}$ 0.8402. n_D 1.4744. Practically insol in water; miscible with alcohol. With dry HCl or HBr it forms monohalides, and with aq HCl or HBr, the dihalide.

d-Form, liquid. bp_{763} 175.5-176°. d_4^{21} 0.8402. n_D^{21} 1.4743. $[\alpha]_D^{19.5}$ +123.8°.

l-Form, liquid. bp_{763} 175.5-176.5°. $d_4^{20.5}$ 0.8407. $n_D^{20.5}$ 1.474. $[\alpha]_D^{19.5}$ −101.3°.

USE: Solvent, manuf resins; wetting and dispersing agent. *Caution:* Skin irritant, sensitizer.

5322. Limonin. *Limonoic acid 3,19:16,17-diactone; 8-(3-furyl)decahydro-2,2,4a,8a-tetramethyl-1H,13H-oxireno-[d]pyrano[4',3':3,3a]isobenzofuro[5,4-f][2]benzopyran-4,6,-13(2H,5aH)-trione.* $C_{26}H_{30}O_8$; mol wt 470.50. C 66.37%, H 6.43%, O 27.21%. Bitter principle of lemon and other *Rutaceae.* Isoln: Bernays, *Ann.* **40**, 317 (1841). Structure and stereochemistry: Melera *et al., Helv. Chim. Acta* **40**, 1420 (1957); Arigoni *et al., Experientia* **16**, 41 (1960); Arnott *et al., ibid.* **16**, 49 (1960); Barton *et al., J. Chem. Soc.* **1961**, 255; Arnott *et al., ibid.* **1961**, 4183. Synthetic studies: Schlatter *et al., Helv. Chim. Acta* **57**, 1044 (1975); Lüthy *et al., ibid.* 1060.



Bitter crystals from methylene chloride + isopropanol or acetic acid, mp 298°. $[\alpha]_D$ −128° (c = 1.21 in acetone). uv max: 207, 285 nm (ε 7000; 38). Slightly sol in water, ether; sol in alcohol, glacial acetic acid.

5323. Linalool. *3,7-Dimethyl-1,6-octadien-3-ol;* 2,6-dimethyl-2,7-octadien-6-ol; linalol. $C_{10}H_{18}O$; mol wt 154.24. C 77.87%, H 11.76%, O 10.37%. $(CH_3)_2C{=}CHCH_2CH_2C(CH_3)(OH)CH{=}CH_2$. Chief constituent of linaloe oil; also occurs in oils of Ceylon cinnamon, sassafras, orange flower, bergamot, *Artemisia balchanorum,* ylang ylang, etc.: Tiemann, *Ber.* **31**, 808 (1898); Walbaum, Stephan, *ibid.* **33**, 2305 (1900); Hesse, Zeitschel, *J. Prakt. Chem.* **66**, 493 (1902); Rafanova *et al.,* U.S.S.R. pat. **103,725** (1956); *C.A.* **51**, 3656c (1957); Naves, *Helv. Chim. Acta* **42**, 1692 (1959). Presence in essential oils: *idem, Compt. Rend.* **251**, 900 (1960). Absolute configuration: Prelog, Watanabe, *Ann.* **603**, 1 (1957). Synthesis of *dl*-linalool: Ruzicka, Fornasir, *Helv. Chim. Acta* **2**, 182 (1919); Surmatis, U.S. pat. **2,848,502** (1958 to Hoffmann-La Roche); Nair, Pandit, *Tetrahedron Letters* **1966**, 5097. *Review:* J. L. Simonsen, *The Terpenes* vol. I (University Press, Cambridge, 2nd ed., 1947), pp 57-68.

l-Form, *licareol.* Colorless liq. bp_{760} 198°; bp_{25} 98-98.3°; bp_{14} 86-87°. d^{20} 0.8622. n_D^{22} 1.4604. $[\alpha]_D^{20}$ −20.1°. Practically insol in water; miscible with alcohol, ether.

d-Form, *coriandrol.* bp_{760} 198-200°; bp_{26} 114-114.5°; $bp_{6.5}$ 93-94°; bp_{12} 86°. d_4^{20} 0.8733. n_D^{20} 1.4673. $[\alpha]_D^{20}$ +19.3°. Soluble in 10 vol 50% alc, 4 vol 60% alc.

dl-Form, bp_{720} 194-197°; bp_{14} 89-91°. d^{15} 0.865.

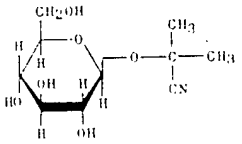
USE: In perfumery instead of bergamot or French lavender oil since it has an odor similar to these oils.

5324. Linalyl Acetate. *3,7-Dimethyl-1,6-octadien-3-yl acetate;* bergamol. $C_{12}H_{20}O_2$; mol wt 196.28. C 73.43%, H 10.27%, O 16.30%. $CH_3COOC_{10}H_{17}$. Most valuable constituent of bergamot and lavender oils, also found in many other volatile oils.

Liquid; bergamot odor. d_4^{20} 0.895. bp 220°. n_D^{20} 1.4460. Insol in water; miscible with alcohol, ether.

USE: In perfumery.

5325. Linamarin. *2-(β-D-Glucopyranosyloxy)-2-methylpropanenitrile;* phaseolunatin. $C_{10}H_{17}NO_6$; mol wt 247.24. C 48.58%, H 6.93%, N 5.67%, O 38.83%. From the seed skins or embryos of flax: Jorissen, Hairs, *Bull. Acad. Roy. Sci. Belg.* [3] **21**, 529 (1891); André *et al., Compt. Rend.* **231**, 590 (1950); Lüdtke, *Biochem. Z.* **323**, 428 (1953). Synthesis: Fischer, Anger, *Ber.* **52**, 854 (1919). Biosynthesis in white clover: Butler, Butler, *Nature* **187**, 780 (1960).



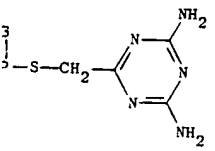
Bitter needles, mp 142-143°. $[\alpha]_D^{18}$ −29°. Freely sol in water, cold alcohol, hot acetone; slightly in hot ethyl acetate, ether, benzene, chloroform; practically insol in petr ether. Evolves HCN with linseed meal but not with emulsin.

Tetraacetate, $C_{18}H_{25}NO_{10}$, needles from alcohol, mp 140-141°. $[\alpha]_D^{14}$ −10.8° (acetone). Sol in acetone, ethyl acetate, chloroform, glacial acetic acid, benzene, warm methanol and ethanol; practically insol in petr ether.

5326. Linarin. *7-[[6-O-(6-Deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-5-hydroxy-2-(4-methoxyphenyl)-4H-benzopyran-4-one;* acacetin-β-rutinoside; linarigenin-glucoside; 5,7-dihydroxy-4'-methoxyflavone-D-glucosido-L-rhamnoside; buddleoflavonoloside. $C_{28}H_{32}O_{14}$; mol wt 592.54. C 56.75%, H 5.44%, O 37.80%. From the flowers of *Linaria vulgaris* Mill., *Scrophulariaceae:* Merz, Wu, *Arch. Pharm.* **274**, 126 (1936); from *Cirsium oleraceum* Scop., *Compositae:* Wagner *et al., ibid.* **293**, 1053 (1960). Structure: Baker *et al., J. Chem. Soc.* **1951**, 691. Synthesis: Zemplén, Bognàr, *Ber.* **74**, 1818 (1941).

Consult the cross index before using this section.

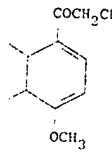
ioic acid O,O-dimethyl ester; S-[(4,6-)methyl] *O,O*-dimethyl phosphorodi-*S-*[(4,6-diamino-*s*-triazin-2-yl)meth-te: 2-dimethoxyphosphinothioylthio-triazine; ENT 25760; PP 175; Saphi-yfos. $C_6H_{12}N_5O_2PS_2$; mol wt 281.32. N 24.90%, O 11.37%, P 11.01%, S



rbank *et al.*, Ger. pat. **1,118,789**, cor-**69,964** (1961, 1965, both to I.C.I.). *n. & Ind. (London)* **1961**, 630.

2°, fp 164-166°. Vapor press. at 25°: soly in water and organic solvents. male rats: 1020, 1450 mg/kg. T. B. *Pharmacol.* **14**, 515 (1969). ricide. *Caution:* Cholinesterase in-

4-Methoxy-6-oxo-1-naphthalenebut-xy-1-naphthoyl)propionic acid; β-(1-propionic acid; γ-oxo-4-methoxy-1-i: Ictéryl. $C_{15}H_{14}O_4$; mol wt 258.26. 24.78%. Prepn: Ruzicka, Waldman, 07 (1932); Fieser, Hershberg, *J. Am.* 1936); Burtner, U.S. pat. **2,623,065**



$_{26}MgO_8$. *Hepalande.*
c.

Md: formerly Mv; at. wt (most 58; at. no. 101; valence 3, also 2. lement. ^{256}Md ($T_{½}$ 1.5 hrs), first nbarding a target of ^{253}Es with heli-on capture to ^{256}Fm: Ghiorso *et al.*, 5). *C.A.* **49**, 12149f (1955). Known 1 ($T_{½}$ 56 days) produced by irradi-: Fields *et al.*, *Nucl. Phys. A* **154**, r of mendelevium is typical of the s to the "tripositive" state (*i.e.*, it e charge); also has the expected ulium, its counterpart in the rare-chemistry of mendelevium: Maly, **58**, 751 (1964). *Reviews:* G. T. *suranium Elements* (Prentice-Hall, 963) 120 pp; C. Keller, *The Chem-Elements* (Verlag Chemie, Wein-pp 595-600; Silva, "Trans-Curium *v. Sci.: Inorg. Chem. Ser. One* vol. University Park Press, Baltimore, *hensive Inorganic Chemistry* vol. 5, . (Pergamon Press, Oxford, 1973) *Handb. Exp. Pharmakol.* **36**, 689-

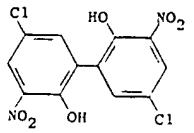
D.$PbCl_2$—lead chloride oxide.

Pogy oil; mossbunker oil. Ob-ast of North America from the *tyrannis*, somewhat larger than a (in the form of glycerides) about nitic acid, 30% linoleic acid, 19% ghly unsaturated).

Reddish oil. Characteristic, distasteful fishy odor and taste. d 0.925-0.933. mp 38.5-47.2°. n_D^{20} 1.480. Sapon no. 191-200. Iodine no. 139-180. Acid no. 3.0-11.6. Sol in ether, benzene, petr ether, naphtha, kerosene, CS_2.

USE: Substitute for linseed oil. In leather dressing formulations. Hydrogenated menhaden oil can be used as a substitute for tallow in soap-making.

5660. Menichlopholan. *5,5'-Dichloro-3,3'-dinitro[1,1'-biphenyl]-2,2'-diol; 4,4'-dichloro-6,6'-dinitro-o,o'-biphenol;* 5,5'-dichloro-2,2'-dihydroxy-3,3'-dinitrobiphenyl; niclofolan; Bayer 9015; Me 3625; Bilevon-M. $C_{12}H_6Cl_2N_2O_6$; mol wt 345.09. C 41.77%, H 1.75%, Cl 20.55%, N 8.12%, O 27.82%. Prepn of analogous 4,4'-bromo compd: Yamashiro, *Bull. Chem. Soc. Japan* **17**, 10 (1942), *C.A.* **42**, 4574b (1948). Anthelmintic activity: Meiser, Federmann, U.S. pat. **3,082,151** (1963 to Bayer); Lane, Stewart, *Vet. Rec.* **80**, 702 (1967).



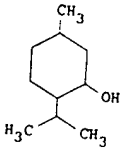
THERAP CAT (VET): Anthelmintic (fasciolicide).

5661. Menisarine. $C_{36}H_{34}N_2O_6$; mol wt 590.65. C 73.20%, H 5.80%, N 4.74%, O 16.25%. From *Cocculus sarmentosus* (Lour.) Diels, *Menispermaceae:* Kondo, Tomita, *J. Pharm. Soc. Japan* **55**, 637 (1935), *C.A.* **33**, 626 (1939). Suggested structure: *eidem, Arch. Pharm.* **274**, 65 (1936); Bick, Todd, *J. Chem. Soc.* **1950**, 1606. Synthetic proof of proposed structure: Tomita *et al.*, *Tetrahedron Letters* **1962**, 635.

Tablets, scales from ether or acetone, dec 203°. $[\alpha]_D^{19}$ +149° (chloroform). Sol in the usual organic solvents, except petr ether; also sol in mineral acids yielding yellow solns.

Hydrochloride, $C_{36}H_{34}N_2O_6$.HCl, yellow needles, dec 279° (after drying at 140°); $[\alpha]_D^{17}$ +172°.

5662. Menthol. *5-Methyl-2-(1-methylethyl)cyclohexanol;* 3-*p*-menthanol; *l*-menthol; hexahydrothymol; peppermint camphor. $C_{10}H_{20}O$; mol wt 156.26. C 76.86%, H 12.90%, O 10.24%. Obtained from peppermint oil or other mint oils, or prepd synthetically by hydrogenation of thymol. Chromatographic sepn from mint oils: Chang, U.S. pat. **2,760,993** (1956 to Iowa State College).



Crystals or granules; peppermint taste and odor. d 0.890. mp 41-43°. bp 212°. n_D^{25} 1.458. $[\alpha]_D^{18}$ −50° (10% alc soln). Sightly sol in water; very sol in alcohol, chloroform, ether, petr ether, freely sol in glacial acetic acid, liq petrolatum. LD_{50} orally in rats: 3180 mg/kg, P. M. Jenner *et al.*, *Food Cosmet. Toxicol.* **2**, 327 (1964).

Note: USP does not distinguish between *l*-menthol and *dl*-menthol.

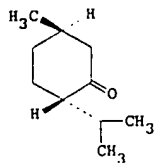
Incompat: Butylchloral hydrate, camphor, phenol, chloral hydrate, Exalgine, betanaphthol, resorcinol or thymol in triturations; potassium permanganate, chromium trioxide, pyrogallol.

USE: In liqueurs, confectionery, perfumery, cigarettes, cough drops, and nasal inhalers.

THERAP CAT: Topical antipruritic.

THERAP CAT (VET): Has been used as a mild local anesthetic; antiseptic; internally as a carminative and gastric sedative.

5663. *l*-Menthone. *(−)-5-Methyl-2-(1-methylethyl)cyclohexanone; l-p-menthan-3-one;* 1-methyl-4-isopropylcyclohexan-3-one. $C_{10}H_{18}O$; mol wt 154.24. C 77.87%, H 11.76%, O 10.37%. Of the four optically active isomers of methone, the one occuring most frequently in nature. Found in various volatile oils, such as pennyroyal, peppermint, geranium: Simonsen, *The Terpenes* vol. I (University Press, Cambridge, 2nd ed., 1947) pp 314-327. Prepd by chromic acid oxidation of *l*-menthol: Hussey, Baker, *J. Org. Chem.* **25**, 1434 (1960); Brown, Garg, *J. Am. Chem. Soc.* **83**, 2952 (1961).



Bitter liq; slight peppermint odor. bp 207°. bp_{41} 116-119°. mp −6°. d_4^{20} 0.895. n_D^{20} 1.4505; n_D^{23} 1.4490. $[\alpha]_D^{20}$ −24.8°; $[\alpha]_D^{27}$ −28.9°. Slightly sol in water; sol in organic solvents.

Note: Apinol obtained by dry distln of wood of *Pinus palustris* Mill. (*P. australis* Michx.), *Pinaceae* is chiefly *l*-menthone: *J. Pharm. Chim.* **18**, 139, 177, 208 (1918), *C.A.* **13**, 569 (1919). Amber-colored oil, bp about 182.2°, d 0.946.

USE: In perfume and flavor compositions.

5664. Menthyl Acetate. *5-Methyl-2-(1-methylethyl)cyclohexanol acetate.* $C_{12}H_{22}O_2$; mol wt 198.30. C 72.68%, H 11.18%, O 16.14%. $CH_3COOC_{10}H_{19}$. Present in peppermint oil.

Colorless liquid, characteristic odor. d_4^{20} 0.919. bp 227°. n_D^{20} 1.4468. $[\alpha]_D^{20}$ −79.42°. Slightly sol in water; miscible with alcohol, ether.

USE: In perfumery; emphasizes floral notes, especially that of rose, used in toilet waters having a lavender odor. Has been suggested for flavoring extracts having caraway or mint flavors.

5665. Menthyl Borate. *5-Methyl-2-(1-methylethyl)cyclohexanol monoester with boric acid.* Estoral. $C_{30}H_{57}BO_3$; mol wt 476.58. C 75.60%, H 12.06%, B 2.27%, O 10.07%. $(C_{10}H_{19})_3BO_3$.

White, tasteless cryst powder; faint menthol odor. Insol in water or alcohol; freely sol in chloroform, ether. Dec into its constituents when in soln.

5666. Menthyl Salicylate. *2-Hydroxybenzoic acid 5-methyl-2-(1-methylethyl)cyclohexyl ester.* $C_{17}H_{24}O_3$; mol wt 276.36. C 73.88%, H 8.75%, O 17.37%. $HOC_6H_4COO-C_{10}H_{19}$.

Clear, yellowish, syrupy liquid; odorless or slight fruity odor. d_{25}^{25} 1.045. Insol in water; miscible with most organic solvents. *Keep well closed and protected from light.*

USE: As a "sun screen" to filter out ultraviolet light in prepns for preventing sunburn.

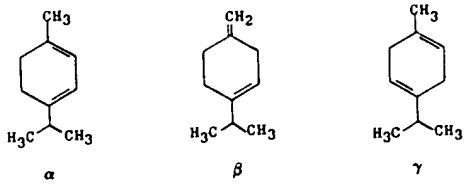
5667. Menthyl Valerate. *3-Methylbenzoic acid 5-methyl-2-(1-methylethyl)cyclohexyl ester; isovaleric acid p-menth-3-yl ester;* Validol. $C_{15}H_{28}O_2$; mol wt 240.37. C 74.95%, H 11.74%, O 13.31%. Contains about 30% free menthol.

Liquid; menthol and valerian odor; cooling, faintly bitter taste. d 0.906-0.908. Insol in water; freely sol in alcohol, chloroform, ether, oils; dec by alkalies.

THERAP CAT: Sedative.

5668. Menyanthes. Buck bean; bog bean; marsh trefoil; water shamrock. Dried leaves or roots of *Menyanthes trifoliata* L., *Gentianaceae. Habit.* Europe, Asia, N. America. *Constit.* Menyanthin.

5669. Meobentine. *N-[(4-Methoxyphenyl)methyl]-N',-N''-dimethylguanidine;* 1-(*p*-methoxybenzyl)-2,3-dimethylguanidine. $C_{11}H_{17}N_3O$; mol wt 207.28. C 63.74%, H 8.27%, N 20.27%, O 7.72%. Antidysrhythmic, antifibrillatory deriv of guanidine, *q.v.* Prepn of the sulfate: R. A. Maxwell, E. Walton, Ger. pat. **2,030,693** corresp to U.S. pat. **3,949,089** (1971, 1976 both to Burroughs Wellcome). Antidysrhythmic effects and tissue concentration: K. B. Touw *et al.*, *Pharmacologist* **19**, 268 (1977); K. B. Touw, *Diss. Abstr. B* **39**, 5340 (1979). Pharmacokinetics by radioimmunoassay: J. W. A. Findlay *et al.*, *Pharmacologist* **21**,



α β γ

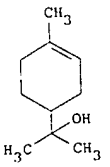
α-Terpinene, oil, pleasant odor of lemons. bp 173.5-174.8°; $bp_{13.5}$ 65.4-66°, $d_4^{19.6}$ 0.8375. n_D^{20} 1.4784. Practically insol in water. Miscible with alcohol, ether.

β-Terpinene, oil, bp 173-174°. d^{22} 0.838. n_D^{22} 1.4754.

γ-Terpinene, oil, bp 183°. d_4^{15} 0.853. $n_D^{15.6}$ 1.4754.

Dihydrochloride, $C_{10}H_{18}Cl_2$, crystals, mp 51-52°.

8996. α-Terpineol. *α,α,4-Trimethyl-3-cyclohexene-1-methanol; p-menth-1-en-8-ol.* $C_{10}H_{18}O$; mol wt 154.24. C 77.86%, H 11.76%, O 10.37%. Terpineol exists as three isomers, α-, β-, and γ-terpineol: J. L. Simonsen, *The Terpenes* vol. I (University Press, Cambridge, 2nd ed., 1947) pp 256-274. Isoln of *d*-α-terpineol from petitgrain oil: Walbaum, Hüthig, *J. Prakt. Chem.* **67**, 322 (1903). Isoln from *l*-α-terpineol from long leaf pine oil: Teeple, *J. Am. Chem. Soc.* **30**, 412 (1908). Isoln of *dl*-α-terpineol from cajeput oil: Voiry, *Compt. Rend.* **106**, 1540 (1888). Synthesis of *d*-α-terpineol: Cologne, Crabalona, *Bull. Soc. Chim. France* **1960**, 102. Synthesis of *l*-α-terpineol: *eidem, ibid.* **1959**, 1505. Stereochemistry: Henbest, McElkinney, *J. Chem. Soc.* **1959**, 1834. *Review:* Wagner, *Mfg. Chemist* **22**, 98, 153 (1951).



d-Form, liquid. $bp_{4.5}$ 81-82°; bp_{731} 206-207°. d_4^{20} 0.9338. n_D^{20} 1.4818. $[\alpha]_D^{20}$ +92.45°. Solidifies at 31°.

Phenylurethan, $C_{17}H_{23}NO_2$, crystals from petr ether, mp 111°. $[\alpha]_D^{20}$ +30.50° (benzene).

l-Form, liquid. bp_5 80-81.5°. d_4^{20} 0.935. n_D^{20} 1.4820. $[\alpha]_D^{20}$ −100° (c = 20 in alc). Solidifies at 36.4°.

Dinitrobenzoate, $C_{17}H_{20}N_2O_6$, crystals from alcohol, mp 101.5°. $[\alpha]_D^{20}$ −31° (c = 9.5 in carbon tetrachloride).

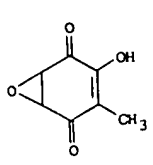
dl-Form, liquid. bp_3 85°; bp_{752} 218.8-219.4°. d^{15} 0.9386. n_D^{20} 1.4831.

Phenylurethan, $C_{17}H_{23}NO_2$, crystals, mp 113°.

USE: Perfumes; denaturing fats for soap manufacture.

THERAP CAT: Antiseptic.

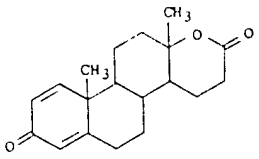
8997. Terreic Acid. *(1R-cis)-3-Hydroxy-4-methyl-7-oxabicyclo[4.1.0]hept-3-ene-2,5-dione;* 2-hydroxy-3-methyl-1,4-benzoquinone 5,6-epoxide; 5,6-epoxy-3-hydroxy-*p*-toluquinone. $C_7H_6O_4$; mol wt 154.12. C 54.55%, H 3.92%, O 41.53%. Antibiotic metabolite produced by the mold *Aspergillus terreus:* Wilkins, Harris, *Brit. J. Exp. Pathol.* **23**, 166 (1942); Abraham, Florey, in H. W. Florey *et al., Antibiotics* vol. I (Oxford Univ. Press, New York, 1949) p 337; Kaplan *et al., Antibiot. & Chemother.* **4**, 746 (1954). Structure: Sheehan *et al., J. Am. Chem. Soc.* **80**, 5536 (1958). Synthesis of the racemate: Rashid, Read, *J. Chem. Soc. (C)* **1967**, 1323. Alternate synthesis and resolution of isomers: Sheehan, Lo, *J. Med. Chem.* **17**, 371 (1974).



(−)-Form (natural), pale yellow plates from benzene or hexane. Easily sublimed *in vacuo.* mp 127-127.5°. Rotation varies considerably with the solvent: $[\alpha]_D^{22}$ −16.6° (chloroform); $[\alpha]_D^{22}$ −28.6° (methanol-benzene 1:1); $[\alpha]_D^{22}$ +74.3° (pH 7 phosphate buffer). uv max (ethanol): 214, 316 nm (log ε 4.03, 3.88). Enol-type acid (pKa 4.5). Slightly sol in water. Soluble in ether, lower alcohols, acetone, hot cyclohexane. Moderately stable to mineral acid, but dec rapidly in alkaline soln. LD_{50} i.v. in mice: 71-119 mg/kg.

8998. Tertiomycins. Antibiotic substances produced by *Streptomyces eurocidicus.* Isoln of *Tertiomycin A* and *Tertiomycin B:* Osato *et al., J. Antibiot.* **8A**, 105, 161 (1955). Tertiomycin A also isolated from *S. albireticuli:* Miyake *et al., ibid.* **12A**, 59 (1959). Manuf by culture of *S. eurocidicus:* Umezawa *et al.,* **Japan.** pat. **5200('67)** (to Sanraku Ocean Co.), *C.A.* **67**, 10386c (1967). Belongs to the erythromycin-carbomycin group of antibiotics.

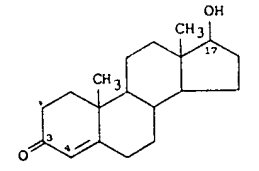
8999. Testolactone. *D-Homo-17a-oxaandrosta-1,4-diene-3,17-dione; 13-hydroxy-3-oxo-13,17-secoandrosta-1,4-dien-17-oic acid δ-lactone;* 1,2,3,4,4a,4b,7,9,10,10a-decahydro-2-hydroxy-2,4b-dimethyl-7-oxo-1-phenanthrenepropionic acid δ-lactone; delta-1-testololactone; 1-dehydrotestololactone; 17α-oxo-D-homo-1,4-androstadiene-3,17-dione; Δ^1-testolactone; NSC-23759; SQ 9538; Fludestrin; Teslac. $C_{19}H_{24}O_3$; mol wt 300.38. C 75.97%, H 8.05%, O 15.98%. Obtained by microbial transformation of progesterone, Reichstein's substance S, or testosterone: Fried *et al., J. Am. Chem. Soc.* **75**, 5764 (1953); *eidem.* U.S. pat. **2,744,120** (1956 to Olin Mathieson); Brannon *et al., J. Org. Chem.* **30**, 760 (1965). Comprehensive description: K. Florey, Ed. in *Analytical Profiles of Drug Substances* vol. 5 (Academic Press, New York, 1976) pp 533-553.



Crystals from acetone, mp 218-219°. $[\alpha]_D^{23}$ −45.6° (c = 1.24 in chloroform). uv max (ethanol): 242 nm (ε 15,800).

THERAP CAT: Antineoplastic.

9000. Testosterone. *17β-Hydroxyandrost-4-en-3-one;* Δ^4-androsten-17β-ol-3-one; *trans*-testosterone; Géno-cristaux Gremy; Malestrone (amps); Orquisteron; Percutacrine Androgénique; Primotest; Primoteston; Sustanon; Mertestate; Testobase; Virosterone; Virormone; Testryl; Testrone; Homosteron; Oreton-F; Teslen. $C_{19}H_{28}O_2$; mol wt 288.41. C 79.12%, H 9.79%, O 11.09%. Principal hormone of the testes, produced by the interstitial cells. Isoln in minute amounts from testes, esp bull testes: David *et al., Z. Physiol. Chem.* **233**, 281 (1935). Prepd by conversion of other steroids such as cholesterol. The important intermediate dehydroandrosterone is efficiently transformed into testosterone by a microbial process: Mamoli, Vercellone, *Ber.* **70**, 470 (1937), and later papers; U.S. pat. **2,236,574.** Structure: Butenandt, Hanisch, *Ber.* **68**, 1859 (1935); *Z. Physiol. Chem.* **237**, 89 (1935); Ruzicka, Wettstein, *Helv. Chim. Acta* **18**, 1264 (1935); and Kägi, *ibid.* **18**, 1478 (1935); Fieser, Fieser, *Steroids* (New York, 1959) *passim.* Structure determn by x-ray crystallography: P. J. Roberts *et al., J. Chem. Soc., Perkin Trans. II* **1973**, 1978.



Needles from dil acetone, mp 155°. $[\alpha]_D^{24}$ +109° (c = 4 in alc). uv max: 238 nm. Insol in water; sol in alcohol, ether, and other organic solvents. 0.015 mg = 1 international unit. LD_{100} i.p. in female rats: 325 mg/kg.

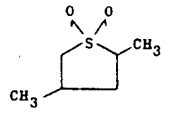
this temp. Vapor density 4.35. Sol in ether, dioxane, acetone, aromatic hydrocarbons. Sparingly sol in carbon disulfide, aliphatic hydrocarbons. LD_{50} orally in rats: 440 mg/kg, Smyth *et al., Arch. Ind. Hyg. Occup. Med.* **4**, 119 (1951).

See also Methyl Sulfate, CH_3OSO_2OH.

Caution: Extremely hazardous. No warning characteristics (e.g. odor, irritation). Delayed appearance of symptoms may permit unnoticed exposure to lethal quantities. Liquid produces severe blistering, necrosis of skin. Sufficient skin absorption can occur to give serious poisoning. Vapors, after relatively asymptomatic latent period, cause severe inflammation and necrosis of eyes, mouth, respiratory tract. Severe and fatal pulmonary damage may result. Systematically causes prostration, convulsions, delirium, paralysis, coma, delayed damage to kidneys, liver, heart with ensuing death in severe cases: E. Browning, *Toxicity and Metabolism of Industrial Solvents* (Elsevier, New York, 1965) pp 713-721. This substance has been listed as a carcinogen by the EPA: *Second Annual Report on Carcinogens* (NTP 81-43, Dec. 1981) pp 129-130.

USE: Methylating agent in the manuf of many organic chemicals: L. Fieser, M. Fieser, *Reagents for Organic Synthesis* (John Wiley, New York, 1967) pp 293-295. War gas.

3253. 2,4-Dimethylsulfolane. *2,4-Dimethyltetrahydrothiophene 1,1-dioxide;* 2,4-dimethylthiacyclopentane 1,1-dioxide; 2,4-dimethyltetramethylene sulfone; 2,4-dimethylcyclotetramethylene sulfone. $C_6H_{12}O_2S$; mol wt 148.24. C 48.62%, H 8.16%, O 21.59%, S 21.63%. Prepd by catalytic hydrogenation of 2,4-dimethyl-3-sulfolene: Morris, Melchior, U.S. pat. **2,451,298** (1948 to Shell).



Colorless to yellow liquid. d_4^{20} 1.1362. n_D^{20} 1.4733. bp_5 123.3; bp 280-281° (some decompn). Miscible with lower aromatic hydrocarbons: partially miscible with naphthenes, olefins, paraffins. Limited miscibility with water.

USE: Solvent for liquid-liquid and vapor-liquid extraction processes.

3254. Dimethyl Sulfone. $DMSO_2$; methyl sulfone; methylsulfonylmethane. $C_2H_6O_2S$; mol wt 94.33. C 25.52%, H 6.43%, O 34.00%, S 34.06%. $CH_3SO_2CH_3$. Has been found in primitive plants such as *Equisetum arvense* L., *Equisetaceae* and in the adrenal cortex of cattle: Pfiffner, North, *J. Biol. Chem.* **134**, 781 (1940). Easily prepd by oxidation of dimethyl sulfide: Douglas, *J. Am. Chem. Soc.* **68**, 1072 (1946); McAllan *et al., ibid.* **73**, 3627 (1951).

Crystals, mp 109°. bp_{760} 238°. Sublimes at 13 mm and 90° to 100°. Infrared absorption (solid) 7.6-8.7 μ. Dipole moment 4.44 (vapor). Freely sol in water, methanol, ethanol, acetone. Sparingly sol in ether.

USE: High temp solvent for many inorganic and organic substances.

3255. Dimethyl Sulfoxide. *Sulfinylbis[methane]; methyl sulfoxide;* DMSO; SQ 9453; DMS-70; DMS-90; Deltan; Demasorb; Demavet; Demeso; Dermasorb; Dolicur; Domoso; Dromisol; Gamasol 90; Hyadur; Infiltrina; Rimso-50; Somipront; Syntexan; Topsym (rescinded). C_2H_6OS; mol wt 78.13. C 30.74%, H 7.74%, O 20.48%, S 41.03%. $(CH_3)_2SO$. Prepd by air-oxidation of dimethyl sulfide in the presence of nitrogen oxides: Smedslund, U.S. pat. **2,581,050** (1952 to Aktiebolaget Centrallaboratorium); Coma, Gerttula, U.S. pat. **3,045,051** (1962 to Crown Zellerbach). Usually obtained as a by-product of wood pulp manuf for the paper and allied industries: Robbins, *Chem. Eng.* **68**, No. 13, 100 (1961). Purification: Traynelis *et al., J. Org. Chem.* **27**, 2377 (1962). Toxicity data: Brown *et al., J. Pharm. Pharmacol.* **15**, 688 (1963); Willson *et al., Toxicol. Appl. Pharmacol.* **7**, 104 (1965). Reviews of pharmacology and toxicology: Jacob, Wood, *Arzneimittel-Forsch* **17**, 1553-1560 (1967); David, *Ann. Rev. Pharmacol.* **12**, 353-374 (1972). *Review:* Ranky, Nelson, "Dimethyl Sulfoxide" in *Organic Sulfur Compounds*, **vol. 1**, N. Kharasch, Ed. (Pergamon Press, New York, 1961) pp 170-182.

Very hygroscopic liquid. Practically no odor or color. Slightly bitter taste with sweet after-taste. d_4^{20} 1.100. mp 18.45° (supercools easily). bp 189°; bp_{17} 83°; $bp_{5.11}$ 56.6°; $bp_{2.82}$ 47.4°; $bp_{0.79}$ 30°; $bp_{0.37}$ 20°. Flash pt, open cup: 203°F (95°C). n_D^{20} 1.4795; n_D^{21} 1.4787. Viscosity at 27° = 1.1 cp. Specific heat 0.7 cal/g (liq). Dielectric constant: 45. Sol in water, ethanol, acetone, ether, benzene, chloroform. Forms stable coordination complexes with metals: Meek *et al., J. Am. Chem. Soc.* **82**, 6013 (1960). LD_{50} orally in rats: 17.9 ml/kg, Bartsch *et al., Arzneimittel-Forsch.* **26**, 1581 (1976).

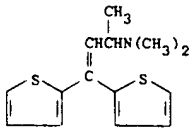
Human Toxicity: Skin contact results in primary irritation with redness, itching and sometimes scaling. Urticarial wheals are not uncommon. Corneal opacities have been produced in exptl animals.

USE: Solvent for acetylene, sulfur dioxide and other gases. As antifreeze or hydraulic fluid when mixed with water. Solvent for Orlon. As paint and varnish remover. Dissolves some hydrocarbons more than others, *see* data sheets issued by Crown Zellerbach Corp., Camas, Wash. Review of use in organic chemistry: Agami, *Bull. Soc. Chim. France* **1965**, 1021-1039.

THERAP CAT: Topical anti-inflammatory.

THERAP CAT (VET): Proposed as analgesic, anti-inflammatory agent, and penetrant carrier to enhance absorption.

3256. Dimethylthiambutene. *N,N-Dimethyl-4,4-di-2-thienyl-3-buten-2-amine; N,N,1-trimethyl-3,3-di-2-thienylallylamine;* 3-dimethylamino-1,1-bis(2-thienyl)-1-butene; 3-dimethylamino-1,1-di(2'-thienyl)but-1-ene; NIH-4542; 338C48; Ohton; Aminobutene; Dimethibutin; Kobaton; Takaton. $C_{14}H_{17}NS_2$; mol wt 263.42. C 63.84%, H 6.51%, N 5.32%, S 24.35%. Prepn: Grignard reaction of ethyl β-dimethylaminobutyrate with 2-thienyllithium and dehydration of the resulting 3-dimethylamino-1,1-di-2-thienylbutanol with HCl: Adamson, *J. Chem. Soc.* **1950**, 885; U.S. pat. **2,561,899** (1951 to Burroughs Wellcome); Brit. pat. **657,301** (1951 to Wellcome Foundation).



Viscous, dark brown or yellow oil, $bp_{0.05}$ 123-125°; bp_3 157-158°. Sol in chloroform, ether.

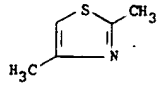
Hydrochloride. $C_{14}H_{18}ClNS_2$, may be recrystallized from mixt of ethyl acetate and ethanol, mp 168-169°. Sol in water, chloroform. LD_{50} orally in mice: 199 mg/kg.

Picrate, mp 169-170°.

Caution: Abuse leads to habituation or addiction.

THERAP CAT: Analgesic.

3257. 2,4-Dimethylthiazole. C_5H_7NS; mol wt 113.18. C 53.06%, H 6.23%, N 12.38%, S 28.33%. Prepd from chloroacetone and thioacetamide: Hantzsch, *Ann.* **250**, 265 (1889); Merck, Ger. pat. **670,131**, *C.A.* **33**, 2909 (1939); Schwarz, *Org. Syn.* **25**, 35 (1945).



Hygroscopic liquid. Penetrating odor. d_4^{15} 1.0601. bp_{719} 144-145.5°. Miscible with ice-cold water, but separation occurs upon warming. Sol in alcohol, ether.

Picrate, prisms, mp 137-138°.

Methyl iodide, crystals, dec 260°.

3258. *sym*-Dimethylthiourea. Dimethylthiocarbamide. $C_3H_8N_2S$; mol wt 104.18. C 34.58%, H 7.74%, N 26.89%, S 30.78%. $CH_3NHCSNHCH_3$.

Colorless, exceedingly deliquesc crystals. mp 60-62°. Very sol in water, alcohol, acetone; sparingly sol in benzene,

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